How Does VC Activism Backfire in Startup Experimentation?

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Abstract

We utilize granular data from the life science sector to study how VC activism affects strategic experimentation decisions. We show that pipeline prioritization, deciding the timing and selection projects to advance, is prevalent in startup growth. Despite more interactions from smaller and more focused VCs, their biotech startups are *less* likely to exit via IPOs. Consistent with such activism prematurely prioritizing the research pipeline, startups backed by concentrated VCs exhibit slower progress in clinical trials and tend to discontinue projects due to pipeline priority rather than financial and quality reasons. For identification, we use limited partners' adoption of ESG objectives as instruments for affected VCs' portfolio attention. Lastly, we highlight conflicting experimentation preferences between general partners and founding teams due to investment horizon and portfolio cannibalization.

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1 Introduction

The strategic experimentation process is inherently embedded in startup growth as a real option problem. Most entrepreneurs face significant uncertainty about the underlying technology, with limited chances of success. While *ex-ante* founders hedge the failure risks by exploring various projects with the core technology, the availability of cash and R&D capital ultimately restricts the number of projects that can be advanced. This paper focuses on this project prioritization decision, where entrepreneurs decide when and which projects to pursue, arguing that active VC oversight exerts control power to influence or even interfere in this process. As a result, the investment and continuation of novel ideas are not determined by a competitive contest about scientific potential. Instead, echoing the widely-cited "Entrepreneurship as Experimentation" perspective by Kerr et al. (2014), these decisions are shaped by "*a myriad of incentive, agency, and coordination problems*" arising from investor relationships.

We utilize granular data from the life science sector to study how VC activism affects strategic experimentation decisions. The key findings are that while smaller and more focused VCs engage more actively with portfolio firms, their involvement can hinder startups' strategic experimentation by prematurely prioritizing the pipeline and holding back many early-stage innovative projects. This value destruction likely reflects the conflicting preferences between the general partners and the founding team. Our findings do not necessarily contradict previous research on the benefits of VC monitoring; rather, they highlight the heterogeneity in the hard-to-observe involvement processes. The notion of VC activism encompasses many activities, and we acknowledge the value-adding channels such as professionalization (Hellmann and Puri, 2002), fundraising (Bottazzi et al., 2008), and recruiting (Amornsiripanitch et al., 2019). We complement these findings by examining how VC involvement influences R&D decisions, echoing the recent concern of Lerner and Nanda (2020) that the VC structure is optimized only for a narrow slice of technological progress. The net effect of VC intervention and engagement depends on a startup's

demand for these various VC services.

In this paper, we focus on VC investments in drug development startups for several reasons. First, VCs are crucial players in the drug development landscape: more than 20% of annual VC funding is allocated to the biotech and healthcare industry, according to a 2023 VC industry report.[1] Second, healthcare VCs insist on control provisions and place greater value on non-human intellectual properties rather than the founding team (Gompers et al., 2020), suggesting that VC activism may backfire due to conflicts with entrepreneurs in this sector. Lastly, our data allows us to observe the experimentation details at the project level. Indeed, Ewens and Sosyura (2023) recently document that losing a VC director has inconclusive impacts on startup patenting activities, highlighting the need for further investigation with more granular measures in the innovation process.

We begin with three stylized facts to clarify the institutional settings of entrepreneurship in the life sciences sector. First, we note the prevalence of pipeline prioritization during the strategic experimentation process of innovative startups. Summary statistics from biotech IPOs in our sample reveal that these companies typically initiate around 12 projects for experimentation. By the time of the IPO, however, over one-third of these projects have been discontinued, with the majority still in the pre-clinical stage. On average, only one project reaches Phase 2, while approximately 1.3 projects advance to Phase 1. These patterns, which are generalizable beyond the life sciences sector, highlight the importance of timing and selection in project prioritization.

Second, guided by the existing literature (e.g Bernile et al., 2007; Matusik and Fitza, 2012), we then characterize a startup's investor activism using two straightforward measures, the size and the concentration of their VC's portfolio. Theoretically, researchers argue that a concentrated portfolio can be beneficial due to the VC activism (e.g. Kanniainen and Keuschnigg, 2003; Fulghieri and Sevilir, 2009). Both academic research and anecdotal evidence suggests that VCs frequently engage with their portfolio companies on

[1]For more details, see the article from Carta on December 19, 2023: https://carta.com/blog/vc-shifts-2023.

financing and operational decisions. However, due to their limited capacity and human capital, expanding the portfolio size and scope may reduce the attention VCs can dedicate to each startup. Consistent with this, we find that more concentrated VCs are more actively involved with their portfolio firms, as indicated by board representation (Lerner, 1995).

Our final documented fact indicates, perhaps surprisingly, that VC activism does not enhance innovation performance in the life sciences sector. Instead, we find that biotech startups backed by VCs with smaller, more focused portfolios in this sector are *less* likely to achieve a successful exit through an IPO. To reconcile these findings, we propose that conflicts of interest can arise when VCs actively engage in prioritization decisions. Given their limited investment horizons and concerns over portfolio cannibalization, VCs may have incentives to delay or even terminate promising projects at an early stage. This argument is best illustrated by the anecdote of Acerta Pharma, an innovator of blockbuster blood cancer drugs, where investors prioritized a quicker project to approval over a potentially more lucrative long-term strategy by replacing the founding team.

To establish direct evidence of engaged VCs holding back scientific experimentation, we use comprehensive project-level development data from Cortellis, tracking the progress of clinical trials across phases in a quarterly panel of approximately 85,000 observations. We follow the previous logic and create two baseline measures for VC activism at the project level, but also explore alternative measures in the robustness check section. The first one is the logarithm of equal-weight portfolio sizes of all VCs investing in a focal project. Consistent with our hypothesis, a one-standard increase in the size measure is associated with an increased chance of progressing by 0.58%, equivalent to 44% the unconditional quarterly progressing rate. Alternatively, we measure the concentration of each VC's investments using the Herfindahl-Hirschman Index (HHI) based on the allocation weights among portfolio startups. Conversely, the coefficients of HHI-based measures are negative and significant, further suggesting that more VC engagement is associated with worse innovation outcomes.

We acknowledge that the screening and selection in VC deals could confound our interpretation of the previous results. Larger and more diversified VCs may endogenously match with higher-quality biotech startups, creating a natural positive correlation between VC size and progress rate. To establish causal evidence, we need to obtain exogenous variations of VC portfolio sizes and diversification while holding the *ex-ante* matched VC-startup pair consistent to alleviate selection and then study the impacts of such variations on project-level innovation outcomes. Our instrument utilizes the staggered adoption of environmental and sustainable investment principles by an important category of VC limited partners (LPs), the state public pension funds. Life science startups are arguably neither green nor brown companies. We confirm that VC financing activities in the biotech sector are not directly affected by the shock, and the exclusion restriction likely holds. The relevance of our instrument is supported by the finding that VCs exposed to sustainability goals significantly reduce investments in "brown firms" in the private market. We further argue that previously diversified VCs must reduce their portfolio size and concentrate their holdings given an environmentally constrained investment opportunity set, shifting their attention towards the life science sector. This is indeed what we observe in the first stage, with t-statistics of the instrument ranging from 3.4 to 6.8 and all F-statistics above 10. Consistent with our OLS results, the second-stage coefficients for size-based measures are positive and significant, while the coefficients for HHI-based measures are negative and significant. These results again suggest that after a life-science startup's existing VCs become more engaged, its R&D efficiency significantly decreases.

We further support the intervention argument through the subset of sample drug projects that are discontinued with disclosed reasons. The data provider categorizes the reasons for discontinuation into four categories: pipeline priority, lack of efficacy, lack of funding, and other reasons. Consistent with our hypothesis, we find that projects are more likely to be discontinued for prioritization when the company is held by more focused VCs. In contrast, we do not find any significant correlations between VC activism and funding-related

or quality-related discontinuation. These null results first alleviate the concern that larger and more diversified VCs may be more lenient in capital provision for financing more costly experimentation. Additionally, lack of financing sufficiency, as demonstrated by Inderst et al. (2007), does not necessarily imply weaker innovation performance because the threat of "shadow pockets" improves entrepreneurial incentives through internal competition among portfolio startups. Besides, we do not find project qualities significantly differ by VC size and concentration, echoing the difficulty investors face in screening novel projects (Kerr et al., 2014).

How can an active VC find project prioritization optimal while the withheld project remains valuable for the startup? We argue that conflicting preferences in prioritization decisions arise between investors and founders due to differences in investment horizons and the risk of portfolio cannibalization. First, in many disease areas, the sequence of clinical trials can take over twenty years to resolve scientific uncertainty. As a result, VCs may need to liquidate their investments before proof-of-concept evidence is realized, suffering an underpricing discount due to information asymmetry. Consequently, despite societal interests, VCs prefer to avoid projects with high uncertainty or prolonged time frames to generate efficacy signals. The direct implication is that VCs would not hold back projects that have produced publicly observed positive signals. Indeed, we confirm that the negative effects of prioritization only hold significantly in the subsample of early-phase (pre-clinical or Phase 1) projects but remain insignificant in later phases. We also find that specialized VCs value monopoly power protections, such as the orphan drug designation that grants additional market exclusivity conditional on approval. Finally, we split the projects into fast or slow disease groups based on the median expected length of experimentation time to reach Phase 3. The cut-off is roughly 8 years, indicating that projects in the lengthy group may expose VCs to underpricing risks. Consistently, the negative relationship between VC activism and trial progress is more pronounced in the slow disease groups.

Second, when a portfolio startup hedges scientific failure risk by exploring multiple disease targets using the focal technology, it increases the likelihood of competing with another commonly-owned startup in the same VC portfolio. This internal competition creates cannibalization through duplicated R&D costs, increased trial requirements, and market power erosion, ultimately hurting the overall valuation at the portfolio level. We find that VC activism instead tends to concentrate all projects targeting a given therapeutic area within a single portfolio startup. A drug project held by more specialized VCs is more likely to see other projects in the same area developed by its own startup, and less likely by commonly-owned competing portfolio firms. The interpretation is that specialized VCs will prioritize projects within a startup's primary field and hold back others, even when they are still scientifically promising, to avoid negative spillovers across the portfolio.

We perform a series of robustness checks on the baseline results. First, we replicate the analysis using each focal startup's lead VC engagement instead of all VC investors, and we document similarly significant results. Besides, our baseline results also incorporate investment-weighted measures to adjust for the heterogeneous control power of each VC. Second, we confirm that our results are robust to defining concentration at the industry or the geography level. Third, while our baseline results use investment information from PitchBook data, we show that all our findings remain robust when using VentureXpert data. Last, we follow the alternative identification strategy by Bernstein et al. (2016), which utilizes the introduction of direct flights as exogenous variations of VC involvement. We find that increased lead-VC activism likely hinders strategic experimentation progress, particularly in the early stages. However, on-site monitoring has positive impacts on progress in late-stage experimentation, where the strategic commercialization of novel projects becomes a more salient strategic decision. This result is consistent with Bernstein et al. (2016)'s findings on the positive impacts on patent issuance, which represents critical market protection strategies in the life science sector.

Our focus on the project prioritization problem aligns with the experimentation view

of entrepreneurship (Kerr et al., 2014; Ewens et al., 2018). VC financing is optimally structured into stages for interim signals, creating a real option problem for the continuation and termination of innovative projects (Bergemann and Hege, 2005; Manso, 2011). Existing theoretical literature argues that VCs may hold up startups for rent exploitation by threatening funding discontinuation, thereby hurting experimentation incentives (Fulghieri and Sevilir, 2009; Inderst et al., 2007). Instead, our paper highlights the distortion in the direction of innovations during this experimentation process, as VCs selectively prioritize projects that match their investment preferences. While this distortion has been noted by Kerr et al. (2014) and Lerner and Nanda (2020), to our knowledge, this paper is the first empirical study to test and confirm this hypothesis. Additionally, related literature documents that VCs may pass business cycle risks to the innovative sector (Nanda and Rhodes-Kropf, 2013, 2017). Howell et al. (2020) find that innovation conducted by early-stage VC-backed firms is of lower volume and quality in recessions. Unlike the financing channel, our paper shows that increased VC involvement could impede radical innovation's progress.

Our paper is also related to the prior research on portfolio size, concentration, and VC engagement. Early evidence suggests that VCs limit both fundraising frequency and fund size (Gompers and Lerner, 1996), and top-performing VCs voluntarily choose to stay smaller (Kaplan and Schoar, 2005). Various research studies the optimal portfolio size using trade-off theories. Larger portfolios can be beneficial due to diminishing returns of advice per firm (Kanniainen and Keuschnigg, 2003), diversification of idiosyncratic risks (Bernile et al., 2007), and *ex-post* bargaining advantage and resource reallocation (Fulghieri and Sevilir, 2009). However, a trade-off exists because a smaller portfolio allows the VC to spend more effort on each startup.[2] While we agree with the aforementioned value-adding services by VC monitoring, our empirical results highlight the heterogeneity of VC activism and suggest that active engagement may backfire in startup experimenta-

[2]Note that Fulghieri and Sevilir (2009) also argues that a small portfolio ensures that VCs will not threaten to divert resources to extract *ex-post* rents.

tion. As a result, trade-off theories may fail to hold in certain sectors. Our results also echo the inconclusive empirical evidence on how VC specialization impacts startup performance. Gompers et al. (2009) shows that when the individual venture capitalist is a specialist, the performance difference between specialized and general VC firms is minimal. Portfolio diversification also encourages managers to take on riskier projects and facilitates knowledge sharing between portfolio firms (Buchner et al., 2017; Humphery-Jenner, 2013; Matusik and Fitza, 2012). None of these papers focus on the strategic experimentation of innovative ideas as we do.

Our paper is also related to the strand of literature on financing novel and radical drug innovation. Existing literature documents the distorted direction of innovation towards short-term and less innovative drugs through two channels. First, Budish et al. (2015) argue that drugs taking longer to complete clinical trials will enjoy a shorter intellectual property right after commercialization due to a fixed patent term. Second, Krieger et al. (2022) show that risk aversion prevents pharmaceutical companies from optimally investing in novel drug development. Unlike their findings, we focus on the conflict of interests between investors and developing companies. Lastly, our paper falls into the broad literature on the impacts of external financing conditions on drug innovations, such as mergers and acquisitions (Cunningham et al., 2021; Phillips and Zhdanov, 2013), IPOs (Aghamolla and Thakor, 2021), and licensing (Hermosilla, 2021; Hammoudeh et al., 2022).

2 Institutional background and Data

2.1 The Life Science Industry

Drug development involves a structured regulatory process that firms must navigate before launching the product on the market. In the US, the FDA evaluates candidate molecule structures (labeled by the generic name of drugs) for specific diseases and symptoms (known as indications) based on their safety and efficacy. The drug development process

consists of several phases. The initial phase involves the discovery stage and pre-clinical stage, where thousands of molecules are screened, and only a few promising candidates undergo testing in laboratories and on animals. Then, drugs move to get tested on human beings. In Phase 1, the safety and efficacy of a drug are evaluated in a small group of 10 to 50 volunteers. If a drug proves safe in humans, it advances to Phase 2 trials, involving a larger sample of 50 to 200 volunteers to evaluate both safety and efficacy. Drugs with robust Phase 2 evidence move on to Phase 3 trials, where safety and efficacy are rigorously tested in a large sample of 200 to 3,000 volunteers.

Developing novel drugs is of high social value, with the COVID-19 pandemic revealing a lack of progress in developing novel drugs and vaccines. Yet, developing drugs is characterized by high research and development costs, lengthy development timelines, and large scientific uncertainty. The average cost of getting a new drug into the market between 2009 and 2018 was $1.3 billion (Wouters et al., 2020). The journey of clinical development time can take from five to more than twenty years, with the median being over eight years (Brown et al., 2022). As of June 2023, according to Cortellis data, less than 18% of drugs that undergo clinical trials ultimately receive approval from the Food and Drug Administration (FDA) by June 2023.

Startups are active drivers in drug development, and the activeness has been increasing over time. As per Pitchbook and Cortellis data, the percentage of new drugs from VC-backed startups rises steadily from 2000 to 2020. The average is 10.43% from 2010 to 2015 and increases to 15.94% from 2016 to 2020. In 2021 alone, Pitchbook-covered biotech companies raised a total of $81.76 billion in VC funding rounds. They assist drug development teams in navigating the "valley of death," an intermediary stage where the science has progressed beyond research funded by federal sources but remains too premature for significant involvement from large pharmaceutical companies. In the life science sector, VC's impact goes beyond financial contributions; they actively engage in the scientific development process (Gompers et al., 2020). For example, Atlas Venture adopted a

venture creation model that assists startups in designing killer experimentation, exploring potential pivots, attracting talents, and assessing market interest from big pharmaceutical companies and other investors.[3]

2.2 Drug development data

We construct a project-level quarterly panel from the Cortellis Drug Discovery Intelligence Platform following Li et al. (2023), Guenzel and Liu (2023), and Krieger et al. (2022). Cortellis aggregates drug data from various public resources, including clinical trial registries, FDA submissions, patent filings, company press releases, financial filings, and other scientific publications. This comprehensive dataset covers the drug's originator company, indications, and both current and historical development status, among other details. Notably, Cortellis provides updates on when an indication progresses to the next clinical phase or is discontinued in the current phase, enabling us to trace the evolution of each indication's development status over time.

Following the institutional convention, each project is a sequence of trials studying a molecule structure's potential for a given indication, i.e. a drug-indication combination. The rationale is that the FDA will separately approve a given product's commercialization targeting various indications. Logically, different diseases require different endpoints and indicators to prove safety and efficacy. Developing companies have to design different sequences of trials for approval. By extracting project-level development records from the Cortellis database, we create a drug-indication quarterly panel documenting each project's furthest active stage (e.g., Phase 1) in a given quarter. Building on the development status, we introduce a dummy variable *Next Phase* as our focal outcome variable to indicate whether the project will progress to subsequent phases in the following quarter. For example, *PRX-8066* is the generic name of a drug developed for multiple types of lung diseases,

[3]For more details, see the article from Fortune on August 15, 2019: The Creation Of Biotech Startups: Evolution Not Revolution.

such as lung infection and MRSA infection. In our panel data, the *PRX-8066*-pulmonary-fibrosis combination is constructed as a separate project from the *PRX-8066*-pulmonary-hypertension combination. In May 2005, the pulmonary hypertension project progressed to Phase 1 clinical from discovery and further progressed to Phase 2 clinical in June 2006. In this case, we code *Next Phase* for *PRX-8066's* pulmonary hypertension project as one at 2005Q1 and 2006Q1. We consolidate three pre-Phase-1 statuses in Cortellis "discovery," "pre-clinical," and "clinical" into a single pre-clinical stage and ignore progressing between pre-Phase-1 statuses. These pre-clinical status designations are more arbitrary decisions by developing companies and may not represent significant scientific milestones. For each project, our quarterly panel includes the quarters when the drug has active trials and excludes records with terminated or perfected development status.[4]

2.3 VC investment data

We obtain data on VC deals from 2000 to 2020 from Pitchbook, which sources private equity, venture capital, and mergers and acquisitions data from regulatory filings, press releases, company websites, financial statements, and industry professionals. For each transaction, the Pitchbook details the investor company, primary investor type, investee company, deal type, investment amount, investment date, type of stock, etc. We collect data VC data from Pitchbook in view of its granularity and accuracy (Chen and Ewens, 2021; Jang and Kaplan, 2023; Fragkiskos et al., 2022; Haltiwanger et al., 2017). In the online appendix, we show that our baseline regression results are robust using the alternative VentureXpert data.

We focus on VC deals made to US startups and exclude non-VC deals, VC deals made by non-VC investors, and VC deals made to companies headquartered outside the US. Next, we match the Pitchbook investee and Cortellis drug companies in the following steps. First,

[4]These statuses include "outlicensed", "no development reported", "discontinued", "withdrawn", "suspended", "pre-registration", "registered" and "launched."

we utilize official company websites to match Cortellis drug companies with Pitchbook startups. Second, we proceed with exact company name matching when website matching is completed. Third, we implement fuzzy matching for company names and manually review all potential matches for those not matched in the above steps. In so doing, we are able to pin down 1,387 unique US drug companies that have ever received VC funds from 2000Q1 to 2020Q4 and also appear in the initial panel we construct in Section 2.2.

We then develop two variables to measure the activism intensity of a VC investor in a given quarter based on its investment activities in the past ten years. The first measure is *Size*, defined as the unique number of startups in which this VC has invested during this window. VCs typically limit the number of startups in their portfolios because they would otherwise devote less time and effort to each company when investing in more firms (Bernile et al., 2007; Fulghieri and Sevilir, 2009). Ewens et al. (2013) argue that the requirement of monitoring efforts restricts the size of the portfolio and the scope of diversification, exposing VC compensations to idiosyncratic risk. We also construct the second measure as a Herfindahl-Hirschman Index (*HHI*) index, reflecting the concentration of a VC's allocation weights across portfolio startups. A VC investor's *HHI* index is the sum of the squares of the percentages of its investments in each drug company over its all investments for drug companies during the 10-year rolling window. Hypothetically, a VC with an HHI of one concentrates all its investment in only one drug company, with smaller HHI suggesting larger portfolios.

In our drug project quarterly panel, each startup may have multiple VC investors in a given quarter. Therefore, we need to aggregate the above measures across various investors at the startup level. For each matched drug company in a given quarter, we track all VC investors that have invested in this company over the past three years and average both *Size* and *HHI* either equally or weighted by the total deal amounts. For example, for drug startup i in a given quarter t, we track all VC deals invested in startup i from quarter $t-11$ to quarter t (three years). If startup i is invested by investor j multiple

times during that period, we aggregate all the investments made by j for weighting purposes. Next, we aggregate the *Size* and *HHI* measures from the startup-VC-quarter level to the startup-quarter level. *Ln(EW-Size)* is the (logarithm of) equally-weighted VC sizes, and *EW-HHI* is the equally-weighted VC HHI index of a given startup at the focal quarter. *Ln(VW-Size)* and *VW-HHI* are similarly defined, except that the corresponding measures are weighted by the total amount of investments in the past three years by each VC. By integrating these startup-level measures with the drug indication development data, we arrive at a drug-indication-quarter panel containing over 90,000 observations on drug indication development status and VC activism intensity measures from 2000Q1 to 2020Q4.

2.4 Other data

The investor base for a startup company usually becomes significantly diversified post-IPO (Bodnaruk et al., 2008), diluting VC's control over the startup. We collect the IPO dates data from SDC Platinum and supplement missing IPO dates with the Jay Ritter's IPO data. After excluding post-IPO records for matched drug companies, the number of observations in our panel reduces to 84,846.

To characterize the oversight from VC investors, we follow Gompers et al. (2023) and Jang and Kaplan (2023) and collect board entrance data for matched drug companies from Pitchbook. Specifically, for a drug company in a given quarter, we check whether there are any new additions to the company's board representing certain VC investors who have previously invested in this company. We then construct a dummy variable *New Board*, which takes the value of one if a drug company gains a new board member from its VC investors in a given quarter and zero otherwise.

2.5 Summary statistics

Table 1 reports the summary statistics for our drug development variables and VC activism intensity measures from 2000Q1 to 2020Q4. Consistent with the scientific difficulty, around 1.3% of the drug indications unconditionally make it to the next phase in a given quarter. The typical drug company in our sample has an average investor size of around 39. If these investors equally invest in all portfolio startups, then the hypothetical average HHI would be around 0.03 ($39 \times (1/39)^2$). Instead, the average weighted HHI is about 0.22, suggesting that VCs rationally allocate additional funding towards certain startups and hold back others in the continuation decisions. Experimentation in the life science sector is costly, with a typical company receiving about $29 million in a three-year rolling window. In the appendix Table IA.1, we split the sample into early-stage (pre-clinical and Phase 1) and late-stage (Phase 2 and Phase 3). The success rate of clinical trials not surprisingly reduces (to 0.8%) in the later phases. Late-stage clinical trials appear to be more expensive, receiving about $31 million every three years.

3 Stylized Facts

In this section, we document three descriptive observations in the life science entrepreneurial sector to motivate and guide our empirical studies. These facts do not necessarily imply causal relations, and we defer more rigorous analyses in later sections. They provide unique institutional knowledge to help us understand the empirical setting.

Fact 1: Life science startups need to prioritize drug projects in the strategic experimentation process before the IPO.

In Table 2, we present the characteristics of drug projects for the startups in our sample that successfully exited by going public. A typical startup actively experiments with ideas, initiating almost 12 projects throughout its pre-IPO life cycle. There are two explanations for this high degree of experimentation. Scientifically, many indications share common

pathways, allowing one molecular structure to be effective for multiple diseases. Additionally, startups explore various projects from a hedging perspective, given the substantial risk of failure in this process. Indeed, about one-third of the projects are suspended by the time of the IPO, resulting in an average active pipeline size of 7.3.

The existence of project prioritization becomes evident when we examine the stages of the active pipeline. The majority of projects (67.1%) do not progress and remain in the pre-clinical phase. On average, a typical IPO startup will have just over one Phase 2 project and 1.3 Phase 1 projects. Progressing a project to Phase 3 is almost impossible for startups. These summary statistics highlight two key aspects of prioritization. First, drug experimentation requires substantial investments in both cash and time, effectively limiting the number of projects that can feasibly progress. Given the significant risk of failure, startups are incentivized to focus resources on the most promising projects based on early evidence from pre-clinical trials. Second, life science IPOs substantially increased following the Jumpstart Our Business Startups (JOBS) Act in 2012. The preference of primary market investors shifted toward biotech companies with products earlier in the FDA approval process (Dambra et al., 2015; Lewis and White, 2023). Most investors value startups based on the leading pipeline's proof-of-concept clinical trials in Phase 1 or dose-ranging Phase 2. Therefore, it is sufficient for life science startups to enter the IPO market, with only a small number of projects moving beyond pre-clinical stages. While project prioritization is a necessary task for life science startups, the optimal timing of prioritization and the choice of prioritized projects are complicated decisions requiring careful consideration.

Fact 2: Smaller and more focused VCs are more actively engaged in overseeing startups in the life science sector.

The literature argues that one benefit of concentrated VC portfolio is to ensure the overseeing efforts of general partners given limited human capital (e.g. Bernile et al., 2007; Fulghieri and Sevilir, 2009). We test this hypothesis in our sample using a simple measure

of engagement in the following regression: whether the startups observe VC investors join their company board.

$$New\,Board_{k,t} = \alpha + \beta VC\,Activism_{k,t} + \Phi X_{k,t} + \gamma_k + \delta_t + \epsilon_{i,j,k,t}, \tag{1}$$

We perform the analysis of Equation (1) at the startup quarterly sample. $New\,Board_{k,t}$ is one if drug company k has any new board members from its VC investors at time t. $VC\,Activism_{k,t}$ indicates the four VC activism intensity measures. Besides company and time fixed effects, we further control for VC investment amounts and a company's active portfolio size in $X_{k,t}$. Table 3 reports the results for estimating Equation (1). The coefficient estimates of *Ln(EW-Size)* and *Ln(VW-Size)* in Columns (1) and (2) are both negative and statistically significant at 5%, suggesting that larger VCs are significantly less likely to take the board seats of their portfolio startups. Consistently, the positive and significant coefficient estimates of *EW-HHI* and *VW-HHI* in Columns (3) and (4) also suggest that VCs with more diversified portfolio companies are less likely to sit on their investing drug company's board. The findings in Table 3 align with recent evidence by Fu (2024), which uses cell phone signals to show that larger VCs monitor less per deal across all industries.

Fact 3: Life science startups invested by more active VCs are *less* likely to exit through IPO.

We wrap up with a simple cross-sectional correlation study linking the previous two facts in our sample. For each startup, we indicate whether it successfully exits by 2020Q4 via the variable *IPO*. Then for both the *Size* and *HHI* measures, we take a simple time-series average to quantify the general degree of VC activism over a startup's life cycle. Figure 1 best visualizes Fact 1 using a simple mean comparison, where we sort all startups into 20 equal-sized buckets. Within each bucket, we calculate the fraction of IPO exits among all startups in it. Panel A exhibits an obvious increasing relation: startups invested by larger funds are more likely to go public. The group of startups held by the smallest VCs exit via IPO by a chance 2.8%, which is eight times smaller than those held by the largest investors

(22.9%). Consistently, the relation is starkly reversed in panels C and D, suggesting that more concentrated VCs see fewer IPOs in their portfolio companies.

There exist many potential non-exclusive explanations for this observation. Larger and more diversified VCs may have sufficient funding and provide additional capital for startups. In Table 4, we explicitly control for the average quarterly investment amounts received by the startup. Indeed, larger capital inflows significantly increase the chance of IPOs. However, the previous relationship remains robust, even controlling for financing amounts. Alternatively, larger VCs may receive better deal flows and match with high-quality startups. In Table 4, we include additional fixed effects such as the initial therapeutic areas, founding times, and locations to absorb the unobserved heterogeneity across startups. For the therapeutic area classification, we follow the International Classification of Diseases 9th Revision (ICD-9), which is a code set used to classify diseases, symptoms, and other factors. Note that Kerr et al. (2014) suggests that even conditional on initial VC investments, it is hard to predict the final success of startups. Moreover, there exists a counterargument to this explanation suggested by Kaplan and Schoar (2005). It is possible that good deals are scarce, and VCs face diseconomies due to decreasing qualities when growing in size. Fund manager human capital is also not easily scalable, and more attentive VCs will arguably spend more time and effort in the screening process. It is ex-ante unclear whether more passive or active VCs will match startups with better qualities.

Summary: Albeit the potential challenges discussed above, the fact that more focused VCs engage more actively complicates the interpretation of Fact 3, suggesting that increased engagement does not necessarily lead to better exit outcomes. To reconcile this, we argue that VC activism can backfire in the strategic experimentation process. Conflicts of interest may arise between the founding team and investors. For instance, VCs may concentrate on a narrow range of drugs that are easier to commercialize in the short term. Due to their limited investment horizons, they might intentionally hold back more radical, yet time-consuming, risky, and innovative projects. Alternatively, VCs may delay

a portfolio startup's project if its progress could cannibalize the pipeline of other startups within their portfolio, thereby affecting the overall valuation of the fund. As a result, even though many projects may seem promising from the startup's perspective, VCs may have incentives to suspend or even terminate them at a very early stage. Consequently, the engagement of active VCs can, in some cases, interfere with the performance and long-term innovation potential of startups.

This conflict is evident in the story of Acerta Pharma, a startup that originated the later-approved blockbuster Bruton's tyrosine kinase (BTK) inhibitor drug acalabrutinib (commercialized as Calquence). Acalabrutinib was initially investigated for multiple blood cancer indications, including mantle cell lymphoma (MCL) and chronic lymphocytic leukemia (CLL). In 2014, the company was considering moving these trials toward Phase 2. The founding CEO wanted to continue the trials of CLL, the most common type of leukemia in adults. However, acalabrutinib's competing drug ibrutinib (Imbruvica) had already been fully approved by the FDA for CLL, and acalabrutinib had to demonstrate significant improvement against ibrutinib in a head-to-head Phase 3 trial for approval. Although the founding CEO was confident in the projected results based on scientific knowledge, this trial would require tracking patient survival for many years. Instead, the lead investor, which was a small fund focusing on blood cancers, wanted to prioritize MCL, a rare disease eligible for accelerated approvals and not requiring comparison with ibrutinib. The founding CEO was ultimately replaced due to the disagreement. In fact, the investors had already forced the CEO to prioritize acalabrutinib in the blood cancer space and move away from autoimmune diseases such as rheumatoid arthritis. This internal turnover held back the overall progress of the startup, leading it to be acquired by the pharmaceutical company AstraZeneca PLC in 2015. Following the prioritization strategy, the FDA granted Calquence accelerated approval for use in MCL in October 2017. However, the initial annual sales were below $100 million due to the small market of MCL as a rare disease. Consistent with the founding CEO's prediction, acalabrutinib successfully completed the

head-to-head Phase 3 trial and received full approval for CLL in November 2019. Sales skyrocketed afterward, with Calquence recording annual sales of $2.5 billion in 2023.

4 Empirical analysis

4.1 Evidence of Project Prioritization

We hypothesize that a higher VC activism intensity will hold back drug project progress during strategic experimentation. A direct implication is that a drug company's projects will become less likely to progress when its VCs are more focused and engaged. We make use of the quarterly project panel from the Cortellis to test this implication. In particular, we focus on the clinical trial progression of drug-indications developed by VC-backed companies and estimate the following baseline regression:

$$Next\,Phase_{i,j,k,p,t} = \alpha + \beta VC\,Activism_{k,t} + \Phi X_{k,t} + \gamma_{i,j} + \delta_p + \zeta_t + \epsilon_{i,j,k,p,t} \tag{2}$$

where $Next\,Phase_{i,j,k,p,t}$ is a dummy variable equal to one if indication i of drug j at phase p from company k enters next phase at time $t+1$. $VC\,Spec_{k,t}$ represents one of the four VC activism intensity measures: $Ln(EW\text{-}Size)_{k,t}$, the logarithmic number of the simple mean of company k's investing VC portfolio sizes at quarter t; $Ln(VW\text{-}Size)_{k,t}$, the logarithmic number of the weighted mean (by investment amount) of company k's investing VC portfolio sizes at quarter t; $EW\text{-}HHI_{k,t}$, the simple average of the HHI index for company k's investing VCs at quarter t; and $VW\text{-}HHI_{k,t}$, the investment-amount-weighted HHI index for company k's investing VCs at quarter t. We control for additional startup-level characteristics that potentially affect project progress in $X_{k,t}$. $Ln(VC\,Amount_{k,t})$ is the logarithmic aggregated investment amount for company k's VC investors at time t, controlling for funding sufficiency. $\#\,Developing\,Drugs_{k,t}$ denotes the number of drugs under active development from company k at time t, controlling for the pipeline size. Besides,

we include granular fixed effects to absorb unobserved heterogeneity at the project level. $\gamma_{i,j}$ is the drug-indication fixed effect, absorbing the scientific potential of each molecule targeting a given therapeutic field. δ_p is the phase fixed effect, reflecting the fact that progressing becomes increasingly difficult in later stages. Lastly, ζ_t is the year-quarter fixed effect, which accounts for time-varying scientific changes. Throughout the paper, we double cluster the standard errors at the ICD-9 and year-quarter level for project-level estimates. In Table IA.2 and Table IA.3, we show that the results remain significant if we replace the ICD-9 clustering with company-level or ICD-chapter level.[5]

Table 5 presents the regression results of Equation (2). Consistent with our predictions, we find that the coefficients of average VC sizes in columns (1) and (2) are positive and significant, suggesting that drug projects backed by larger VCs are more likely to pass clinical trials. Economically, a one-standard-deviation increase in the *Ln(EW-Size)* (i.e., 1.15 units increases in the sample) increases the chance of progressing to the next phase for drug projects developed by VC-backed drug companies by 0.58% ($= 0.005 \times 1.15 \times 100\%$), equivalent to 44% of the unconditional average probability of progressing to next phase. Conversely, the coefficients of average *HHI* in columns (3) and (4) are negative and significant, further suggesting that less VC concentration is associated with better innovation outcomes. Overall, these results support the interpretations that VC activism interferes with their portfolio company's project progressing.

Other confounding characteristics of VCs could have driven the above results. For example, larger and more diversified VCs may be more reputable and have high-quality human capital. As a result, they observe better deal flows and match with better startups. Alternatively, they may have deeper pockets and support more expensive and advanced research designs. The ideal experiment is to hold the VC-startup matched pair constant to alleviate the ex-ante sorting concerns and then exogenously let the VC investors become

[5]The ICD-chapter is a group of ICD-9 codes that share broader medical similarities. For example, Vitamin A deficiency (ICD-9 264) and Vitamin D deficiency (ICD-9 268) all belong to the chapter "Nutritional Deficiencies."

more active and study the downstream effects on innovation progress. To implement this research design, we make use of an instrument variable (IV) analysis. Our instrument utilizes the state-level variation in incorporating environmental and sustainable principles into their public pension funds' investment process. Public pension funds have been active in socially responsible investments for a long time for various reasons (Hong and Kacperczyk, 2009; Dimson et al., 2015). Sixteen states explicitly started to include sustainability in their investment goals in a staggered fashion from 2013 to 2020. This emerging trend in investment practices has incurred a significant impact, ultimately leading to a 2023 March Senate bill trying to prevent pension fund managers from including factors such as climate change in their investment decisions. President Biden later rejected this bill as the first veto of his presidency.

Below, we explain how we construct the instrumental variable based on the variation in adopting sustainability as an investment goal. First, in a given year, we hold each focal drug company's VC investors constant, keeping those who had invested before any sustainability shock exposure. In other words, if a biotech company is first invested in by a VC after an LP shock, we exclude this investor from the instrument construction. Second, for each remaining VC, we determine whether at least one of its LPs has adopted a sustainability goal by a given year. Lastly, we weight the VC-level treatment status at the drug company level by calculating the fraction of treated investors over all holding VCs, thereby creating the instrument *Weighted Exposure*.

We argue that our IV is relevant given the fact that state public pension funds are among the most important LPs in the venture capital industry due to the adoption of prudent investor rules (González-Uribe, 2020). Political agendas driven by state pensions directly impact investment decisions made by general partners (Andonov et al., 2018). While there has been considerable debate in the literature about how investors implement sustainability, particularly in choosing between divestment and engagement in the public equity market (e.g. Berk and Van Binsbergen, 2021; Edmans et al., 2022), it remains an

open question how VCs respond to their LPs' sustainability goals in the private market. Relevant to the first stage of our identification strategy, we present descriptive evidence on the investment strategy changes of the "treated" VCs in our sample in Table 6. These VCs significantly decreased investment activities in the energy sector, both in terms of the number of firms invested in (by 2.1%) and the amount of capital allocated (by 6.2%), indicating a holding reduction strategy. We believe this result aligns with the different sustainable investment strategies employed by state pensions in the public versus private markets. For example,[6] MainePERS takes a passive approach in the public market by holding index funds and relying on the ability to "actively engage with company management, particularly through the proxy voting process." In contrast, before investing with any private asset manager, MainePERS completes a due diligence checklist of ESG-specific items, identifies and monitors risk factors, and requires and reviews an ESG policy from the funds. Indeed, Duevski et al. (2023) document that PE firms experiencing environmental incidents face difficulties in future fundraising. However, readers should interpret this result with caution. The optimality and real effect of this response are beyond the scope of this paper. We only document the before-and-after changes of "treated" VCs investing in the life science sector as it pertains to the interpretation of our first stage. We leave a full-fledged study of this question to future research.

Following the previous result, we hypothesize that VCs exposed to sustainability goals become more constrained in their investment opportunity sets as they seek to avoid investing in "brown firms." This constraint forces these investors to concentrate their portfolios on a smaller number of startups. Notably, this concentration is not solely a result of shifting away from the energy sector. As Figure 2 shows, 5 out of the 7 sectors, with 2 being statistically significant at the 5% level, experience a reduction in the number of startups being invested in. Table 7 reports the 2SLS regression results using instrumented VC activism intensity measures. The first four columns present the first-stage results. In line

[6]For details, see the "Environmental, Social, and Governance Report," 2017 Edition by MainePERS.

with our expectation, all four columns report significant coefficients with predicted signs, suggesting that the exposure to the pension funds' ESG investment requirements has a positive impact on VC concentration, both in terms of the number of firms and the HHI measures. The t-statistic for our IV is between 3.4 and 6.8 across the four first stages, with F-statistics all above 10. These tests provide strong support for the relevance condition.

The exclusion restriction condition requires that after a VC firm's state pensions adopt sustainable investment, this adoption affects the innovation process of that VC's portfolio firms only through activism. Our instrument mirrors the shareholder "distraction" measure in Kempf et al. (2017). They define investor distraction for each firm as its shareholders' portfolio holdings in *other industries* experience substantial shocks, documenting that distraction temporarily reduces monitoring for the focal firm. Instead, we utilize the fact that a biotech startup's VC investors will shift their attention away from "brown firms" if they face sustainability pressures from state pension LPs and allocate that attention toward life science firms. The key challenge to our exclusion restriction is that this shift in investment interest might be associated with a capital influx into life sciences, leading to two concerns. First, existing biotech startups may receive additional funding to support more expensive trials. Second, being forced to concentrate on life sciences, affected VCs may invest in new firms of lower quality. However, the life science sector is arguably neither green nor brown. Table 6 shows that the investment activities by affected VCs do not significantly change in biotech startups, with the only statistically significant increases observed in the financial sector. Thus, we do not find significant evidence that affected VCs are investing more in existing firms or exploring new companies. Moreover, even if affected VCs did supply additional capital to the remaining portfolio biotech startups, we would expect better innovation outcomes associated with concentration. Our hypothesis predicts the opposite, so this channel works against us. To further alleviate this concern, we test whether VC activism intensity affects drug project discontinuation due to lack of funding or lower quality, and find that it does not, as shown in Table IA.4.

Columns (2), (4), (6), and (8) present the second-stage results for drug development status with instrumented VC activism intensity measures. Consistent with our baseline results in Table 5, the coefficients for size-based measures are positive and significant while the coefficients for *HHI*-based measures are negative and significant. For comparison, their magnitudes are much greater than the corresponding OLS estimates. Jiang (2017) shows that it is common for IV estimates to be much larger than their OLS counterparts. This magnitude change in our paper is likely due to differences between local average treatment effects (LATE) captured by the state pension shocks in the 2SLS framework and average treatment effects (ATE) captured in the OLS regressions. We argue that our IV compilers are the VCs that have to respond to the sustainable investment requirement by shifting away from brown industries. Previously, these VCs tended to be generalists with investments spanning both the energy, for example, and life science sectors. Following the shock, they would allocate additional oversight towards biotech firms, potentially diverting human capital that was previously used to monitor the energy sector. However, these new managers may lack the necessary expertise, leading to substantial intervention in project prioritization. As a result, we expect to observe a larger LATE among these compilers.

We interpret the above findings as active VCs holding back innovative projects prematurely in the priority prioritization process. To further support this interpretation, we examine the reasons why startups discontinue an innovative drug project. To be specific, the Cortellis database collects the reasons for drug indications that have ever experienced discontinuation and categorizes them into pipeline priority, lack of funding, and lack of efficacy, if possible. Note that VC-induced project prioritization does not necessarily lead to the actual suspension of projects. Many projects, as in the CLL case in the BTK inhibitor example, are temporarily shelved and progress slower (when they are resumed later). In other cases, projects effectively become "zombie projects" without any trial announcements. However, we could not track the exact timing and the rationales of these temporary holds or silent failures. Instead, we perform a cross-sectional regression in the

subsample of projects ending up being explicitly discontinued. In our project sample, there are 305 initial projects being discontinued from 2000Q1 to 2020Q4. Lack of funding is the most common reason accounting for 27% of all discontinuations, with lack of efficacy and pipeline priority contributing 13% and 15% respectively. In total, around 55% of all the projects have explicit reasons, and we group the remaining projects into the "unknown reason" category.[7] We perform the following regression:

$$Reason_{i,j,k,t} = \alpha + \beta VC\ Activism_{k,t} + \Phi X_{k,t} + FEs + \epsilon_{i,j,k,l} \tag{3}$$

Conditional on a project of drug j in indication i terminated by company k at quarter t, $Reason$ indicates whether it is suspended for a particular reason. The focal regressors are defined similarly in Equation (2). Since each project only has one observation upon discontinuation, we are no longer working on a panel sample, constraining us from including the same set of fixed effects. Instead, we include the ICD-9 fixed effects to absorb the heterogeneity of research difficulty across different therapeutic categories. We also include the startup founder year and location fixed effects to absorb the impacts from startup seniority and R&D clusters. In the control variables, we include VC financing amounts and the number of indications targeted for the drug. The later captures the degree of experimentation at the molecule level.

Table 8 reports the regression results for drugs discontinued due to pipeline priority. The outcome variable is one if the project is discontinued because the developing company wants to prioritize the development of other projects and zero otherwise. We find the coefficient estimates of size-based measures are negative and significant at the 5% level, suggesting that less active VCs are associated with fewer projects discontinued due to pipeline priority. Further, the coefficient estimates of HHI-based measures are positive and significant at the 10% level. The broad implication is that less engaged VCs have a lower

[7] In the regression sample, a few observations are dropped due to being singleton observations with fixed effects. The distribution is similar: lack of funding (24%), pipeline priority (15%), and lack of efficacy (17%).

chance to intervene in the prioritization of the pipeline.

Table IA.4 presents the regression results for drugs discontinued due to lack of funding or efficacy. Figure 3 summarizes the results by plotting the coefficients and confidence intervals of the four VC activism intensity measures for all three categories. First, we do not find any significant relation between activism and lack of funding. In Panels (a) and (b), larger VCs seem to be associated with more financing-induced discontinuations, although the estimates are highly insignificant and the magnitudes substantially reduce in Panels (c) and (d). This suggests that there exists no evidence that startups invested by smaller funds are financially constrained. Secondly, VC activism intensity does not correlate with the lack of efficacy at all, suggesting that even professional investors have difficulty distinguishing project qualities. These null results help rule out the alternative interpretation that larger VCs contribute to drug project success by providing funding and they are better at screening projects. Overall, these results suggest that active VCs intervene in the drug development process mainly through project prioritization.

4.2 Economics of the Conflicts

We argue that VC activism and engagement lead to premature project prioritization due to conflicts of interest between investors and founders. What are the economics behind these conflicts? We argue that conflicting preferences arise between investors and founders due to differences in investment horizons and the risk of portfolio cannibalization. Active VCs, due to their attentiveness, are more likely to recognize and respond to these conflicting preferences. Besides, the marginal benefits (per startup) of reducing costly investments or avoiding negative spillovers are greater for VCs with more concentrated portfolios. As a result, we expect these conflicts to emerge more frequently with increased VC activism.

First, while the founding team aims to maximize the startup's value over their careers, VCs operate with a much shorter investment horizon due to the 10-year contractual structure. Without information asymmetry, this mismatch in horizon would not matter: even

if VCs exit earlier, they would be compensated based on the fairly discounted value of the startup. However, investments in innovative startups, particularly in the life science sector, feature substantial uncertainty and a high degree of information asymmetry. As outsider investors cannot distinguish between good and bad startups, they will impose an underpricing discount for high-quality projects in the pooling equilibrium (Akerlof, 1978). Consistent with this argument, Barrot (2017) shows that VC funds with a longer remaining horizon select younger companies at an earlier stage of their development. Thus, we hypothesize that VCs prefer projects that can generate publicly observable signals as soon as possible within a limited time horizon. A direct implication is that VCs would not hold back projects when their uncertainty has been substantially reduced. The most straightforward public signals about project quality are the progressions across phases. Therefore, we first divide the sample into two subsamples based on whether a drug project has progressed to a certain stage: (1) an early-stage subsample that consists of pre-clinical stage and Phase 1 clinical trial records, and (2) a late-stage subsample that consists of Phase 2 and Phase 3 clinical trial records. The rationale is that having passed Phase 1, most projects would have completed proof-of-concept trials, demonstrating the efficacy of treatments to the public. Furthermore, it takes more time and involves more risk for drug indications in the early-stage subsample to successfully pass all trials compared to those in the late-stage subsample. As a result, we expect the project prioritization effects to hold more strongly among early-stage drug projects.

Table 9 confirms this prediction by reporting the regression results for these two subsamples. We document that significant effects only exist in early-stage drug project samples, as shown in Panel A. In comparison, the estimated coefficients in Panel B are all insignificant. Indeed, we have lower statistical power in Panel B due to fewer late-stage project observations. However, the economic magnitudes are also significantly different. For example, the coefficients of HHI-based measures in Panel A are almost twice as large as those in Panel B.

Besides the obvious signals of scientific progression, there are other indicators of commercialization potential through the FDA designation system. The most established program is the orphan drug designation, which rewards the novel development of treatments for rare diseases through extended market exclusivity after approval. These designations thus become good indicators of projected monopoly power and FDA's endorsement of technology potential. In Table 10, we perform a subsample test based on whether a drug indication has obtained the orphan drug designation.[8] Similarly, we document that coefficient estimates are statistically significant only in drug indications without any regulatory designations, as shown in Columns (5)-(8). Not only are the coefficients not statistically significant in the first four columns, but the signs are also completely the opposite, suggesting potential preferences of active VCs for these designated programs.

While it is straightforward for active VCs to reduce *ex-post* prioritization once the uncertainty has been resolved, we argue that they would also rationally hold back projects with *ex-ante* longer periods to progress. The logic is that VCs expect that the public progression signals are likely to arrive beyond the contractual window, exposing them to underpricing risks. So, we sorted the sample into two subsamples based on the average trial length of each drug indication (at the ICD-9 level). In particular, we leverage all drug development information from the Cortellis database and calculate the average quarters that it takes for all projects in each ICD-9 clustering 2 level from the commencement of the early phase to the completion of the Phase 3 clinical trial. We then code indications from ICD-9 classifications that have developing lengths below (above) the median as "fast (slow) ICD-9" indications.

Table 11 reports the regression results for these two subsamples. We indeed find that coefficient estimates on the VC activism intensity measures are all statistically significant at 1% level among the slow ICD-9 drugs. As shown in Columns (5) and (6), the coefficients of the size-based measures are two times larger than those in the fast ICD-9 subsample

[8]Due to data limitations for project regulatory designations, our sample period for orphan drug designation analysis ends in 2018Q2.

(Columns 1 and 2). Meanwhile, statistical significance drop substantially in the first four columns, even with a more balanced subsample split compared to the previous two tables. The first two columns are insignificant and Columns (3) and (4) are only significant at 10% level.

The second conflict arises from the externalities within portfolio startups. From each startup's perspective, it hedges technology failure risks by exploring multiple indications using the focal molecule. This diversification, however, can negatively impact VC portfolio management by increasing the likelihood that two commonly-owned startups compete in the same disease areas. VCs want to avoid this internal competition for several reasons. First, the FDA awards market exclusivity to each newly approved drug, blocking similar technologies from entering the same therapeutic area for many years. Jointly investing in late-stage competitors can lead to duplicated R&D costs. Second, although competing startups can use different technologies, their research progress can cannibalize each other's chances by raising the bar for FDA approval. As seen in the previous Acerta Pharma example, drug developers often need to demonstrate significant efficacy improvements over state-of-the-art technology. Therefore, the breakthrough of one portfolio company may increase the trial difficulty for others. Finally, even if all the competing projects can be approved, then they will erode each other's potential market power. Consequently, while the startup values the continuation of additional projects, VCs may view them as diverting resources from the primary indication and potentially undermining portfolio value. Consistently, Li et al. (2023) document that after a portfolio drug progresses into Phase 2, VCs tend to redirect other portfolio startups' competing pipelines into different areas.

The implication of the second conflict is that active VCs may prefer each startup to focus on a primary therapeutic area. To test this hypothesis in Table 12, we first identify all additional projects within the same ICD category held by a focal project's VC investors. These projects can either belong to the focal project's own developer or to commonly-owned competing startups. We then normalize the number of projects in each group by the

total number of (all-ICD) projects invested in by the VCs, creating the variables *Own Share* and *Competing Share*, respectively. To interpret our results, it is mostly straightforward to focus on the coefficients of HHI-based measures in Table 12. Columns (3) and (4) suggest that startups held by more concentrated VCs tend to focus on a specific disease, as indicated by a higher fraction of projects developed by themselves in the same area. Conversely, VC activism intensity is associated with a smaller fraction of competing projects from commonly-owned startups in Columns (7) and (8). The coefficients of size-based measures align with this interpretation.

4.3 Robustness checks

We perform a battery set of robustness checks. We validate the findings by focusing only on the lead VC investor, defining the concentration at industry and geographic measures, extracting investment date from an alternative database, and using an alternative measure of VC monitoring.

First, in the previous results, we focus on the activism of all VC investors of the focal startup. The alternative empirical design is to focus on the lead VC investors, as they arguably have the most significant control power to navigate the experimentation process. We benchmark our results using all the VCs as the Pitchbook data itself has substantial missing observations in the lead VC indicator and we have to infer the lead status by cumulative investment amounts. Meanwhile, our value-weighted measures utilize a three-year rolling window investment amounts to capture the relative importance across active investors. One may argue that the three-year window is too short or the investment weights do not proportionally capture the control power. Instead, Table IA.5 repeats the analyses focusing solely on the activism of the lead VC investor. For any given quarter, the lead VC investor is defined as the one who has made the most investment in the startup over the past five years. Consistent with the results in Table 5, the positive coefficient of *Ln(Lead VC Size)* and negative coefficient of *Lead VC HHI* suggest that a more active lead VC impedes

the progress of clinical trials.

Second, one baseline measure of VC activism intensity uses the concentration of allocation weights across individual firms. We construct the startup-level HHI measures as we focus on the VC activism channel: even when VCs diversify within the life science sector by holding more biotech startups, the average intervention on each firm still tends to reduce. In Table IA.6 and Table IA.7, we confirm that our results hold with alternatively defining concentration at the industry or headquarters location level.

Third, we test whether our results are robust to using alternative data sources. We recollect VC investment data from VentureXpert data, re-construct VC activism intensity measures with VentureXpert deals, match Cortellis drug companies with VentureXpert investees and replicate our baseline results. Table IA.8 reports the results for Equation (2) with VentureXpert data. We have slightly more observations when using VentureXpert data since VentureXpert might misclassify PE deals as VC deals. Nevertheless, all columns (1)-(4) are consistent with those in Table 5. Hence, our baseline findings are robust to the alternative VC data source (or, in other words, our baseline results are not driven by different coverage of VC deals).

Lastly, we interpret our main results through the channel that the VC activism interferes with the strategic experimentation process. Our identification strategy utilizes the exogenous variations of VC portfolio construction due to LPs' investment policy. A related strategy is to follow Bernstein et al. (2016) and leverage the introduction of direct flights between the headquarters of drug companies and their lead VC investors as an exogenous shock for conducting on-site engagement. To do so, we identify nearby airports for each drug company and its lead VC investors by those located within 50 miles of driving distance from headquarters city centers. We then collect monthly airline route data from the T-100 Domestic Segment Database from 2000 to 2020, maintained by the Bureau of Transportation Statistics (BTS), and construct a dummy variable to indicate the availability of direct flights between drug company k and its lead VC investors at quarter t. $Direct\,Flight_{k,t}$

equals one if there is at least one flight per week with at least 100 seats available between any pairs of company k's nearby airports and its lead VC's nearby airports by quarter t, and zero otherwise. Among the 1,397 unique drug companies in our baseline sample, 257 experienced the introduction of new direct airlines originating from their lead VC investors from 2000 to 2020.

To evaluate the effects of VC engagement intensity on drug development progress, we employ the difference-in-difference (DiD) approach with the following regressions:

$$Next\,Phase_{i,j,k,p,t} = \alpha + \beta Direct\,Flight_{k,t} + \Phi X_{k,t} + \gamma_{i,j} + \delta_p + \zeta_t + \epsilon_{i,j,k,p,t}. \quad (4)$$

Equation (4) is almost the same as Equation (2), except that we replace the focal regressors with $Direct\,Flight_{k,t}$.[9] Given that $Direct\,Flight_{k,t}$ is time-variant and only turns on after a lead VC investor gets treated, β should be viewed as the DiD coefficient. Since OLS regressions with two-way fixed effects (TWFE method) similar to Equation (4) are the workhorse models for staggered adoption research designs, we first report our results using the TWFE method in Columns (1), (3), and (5) of Table IA.9. Nevertheless, recent literature has shown that the estimates of such equations are consistent only with strong assumptions about homogeneity in treatment effects (Sun and Abraham, 2021; Baker et al., 2022). So we re-estimate the dynamic treatment effects with the interaction weighted (IW method) estimator proposed by Sun and Abraham (2021) and report the average treatment effects from IW estimators in Columns (2), (4), and (6).

Columns (1) and (2) of Table IA.9 report the results based on Equation (4) in the full sample. The coefficient estimates of β are negative in both columns and statistically significant at a 5% significance level in Column (2). Figure IA.1 plots the coefficient dynamics, exhibiting the absence of any pre-trends. These results suggest that when increased lead-VC activism likely hurts the strategic experimentation process, following the direct flight

[9] We also add the control variable for the number of quarters since the first investment of the startup ("# Quarters since first inv") as Bernstein et al. (2016) have a similar variable to control for startup age.

introduction. Inspired by Table 9, we split the full sample into early-stage and late-stage projects. We document conclusive negative effects in the early-stage subsample as shown by the negative and significant coefficients of β in both Columns (3) and (4). On the other hand, the effect of VC monitoring on late-stage clinical trial progress, if anything, is mixed.

Our results do not necessarily contradict with Bernstein et al. (2016), as only 5.6% of their sample companies are in the life science sector. Besides, drug companies frequently adopt an "evergreening" strategy, in which they patent small modifications of existing molecules to extend the potential market power of existing products (Hemphill and Sampat, 2012; Li et al., 2021). So patents also reflect strategic marketing decisions in late-stage trials. We do find positive effects, though insignificant, after the treatment among Phase 2 and 3 projects in Figure IA.1. Overall, the analyses suggest the heterogeneous roles of VC activism in R&D. Excessive engagement may lead to premature withholding of early-stage projects. However, more monitoring might be beneficial to the commercialization of late-stage projects.

5 Conclusion

This paper highlights the heterogeneity in the real effects of of VC activism. By utilizing granular data from the life science sector, we explore an understudied aspect of VC engagement in startups' strategic experimentation processes: project prioritization. Contrary to the common wisdom that VC oversight inherently leads to superior innovation outcomes, we document that startups backed by smaller and more concentrated VCs, while being more engaged, exhibit slower progress in clinical trials. We observe that active VCs tend to prematurely hold back early-stage innovative projects, focusing instead on a narrow range of novel technologies.

Our results underscore the conflicts of interest between investors and founders during the strategic experimentation process. The limited-horizon investment structure of

VCs may force them to focus on projects that are easier to commercialize in the short term, despite the societal impacts of other long-term projects. This preference of VCs could potentially stifle high-risk, novel projects with radical innovations. Moreover, VCs tend to concentrate all projects targeting a given therapeutic area on a single startup to avoid internal portfolio cannibalization. Our findings highlight the heterogeneity in the VC engagement process and provide a more balanced view of its influences alongside the documented benefits from prior literature. Lastly, this paper provides new insights into the impact of VC financing on the direction of technological progress. The limitations of VC financing call for a more nuanced approach to fostering radical innovation in industries where scientific progress is more pervasive.

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Table 1: Summary statistics

This table reports the summary statistics of project quarterly data in our sample from 2000Q1 to 2020Q4. The unit of observation is a drug-indication×year-quarter combination. The number of observations, mean, standard deviation, 25th percentile, median, and 75th percentile of the following variables are displayed: *Next Phase* is a dummy variable equal to one if the drug indication is going to progress to the next phase in the following quarter, and zero otherwise; *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI* is the investment-amount-weighted HHI index for a drug company's investing VCs; *VC Amount* is the aggregated investment amount for a drug company's VC investors in the past three years; *# Developing Drugs* denotes the number of drugs under active development from a drug company. The project development status data is collected from Cortellis. The IPO dates for drug companies are sourced from SDC Platinum and supplemented by Jay Ritter's IPO data. The VC investment data to construct VC activism intensity measures is collected from Pitchbook.

	Obs.	Mean	STD	p25	p50	p75
Next Phase	84,846	0.013	0.114	0.000	0.000	0.000
EW-Size	84,846	39.121	41.469	12.500	28.696	50.500
Ln(EW-Size)	84,846	3.148	1.151	2.526	3.357	3.922
VW-Size	84,846	40.231	43.665	12.286	29.500	52.000
Ln(VW-Size)	84,846	3.161	1.164	2.508	3.384	3.951
EW-HHI	84,846	0.224	0.222	0.069	0.143	0.296
VW-HHI	84,846	0.221	0.223	0.067	0.137	0.291
VC Amount (in millions)	84,846	29.140	41.330	6.000	16.604	37.688
Ln(VC Amount)	84,846	16.392	1.497	15.607	16.625	17.445
# Developing Drugs	84,846	6.995	6.068	3.000	5.000	9.000

Table 2: Pipeline summary statistics of life science IPOs

This table reports the pipeline summary statistics of drug companies exiting via IPOs from 2000Q1 to 2020Q4. The unit of observation is each drug company. The number of observations, mean, standard deviation, 25th percentile, median, and 75th percentile of the following variables are displayed: *# Projects Ever* is the number of projects that a drug company has ever initiated over the sample period; *# Projects Active Upon IPO* is the number of active projects from a drug company upon its IPO; *# Pre-clinical Projects Upon IPO* is the number of projects in the pre-clinical stage from a drug company upon its IPO; *# Phase-1 Projects Upon IPO* is the number of projects in Phase 1 from a drug company upon its IPO; *# Phase-2 Projects Upon IPO* is the number of projects in Phase 2 from a drug company upon its IPO; *# Phase-3 Projects Upon IPO* is the number of projects in Phase 3 from a drug company upon its IPO; *% Projects Suspended before IPO* is the percentage of projects suspended by a drug company before its IPO; *% Pre-clinical Projects Upon IPO* is the percentage of active projects in the pre-clinical stage from a drug company upon its IPO; *% Phase-1 Projects Upon IPO* is the percentage of active projects in Phase 1 from a drug company upon its IPO; *% Phase-2 Projects Upon IPO* is the percentage of active projects in Phase 2 from a drug company upon its IPO; *% Phase-3 Projects Upon IPO* is the percentage of active projects in Phase 3 from a drug company upon its IPO. The project development status data is sourced from Cortellis. The VC investment data to construct VC activism intensity measures is collected from Pitchbook. The IPO dates for drug companies are sourced from SDC Platinum and supplemented by Jay Ritter's IPO data.

	Obs.	Mean	STD	p25	Median	p75
# Projects Ever	258	11.783	10.185	5.000	8.000	15.000
# Projects Active Upon IPO	258	7.275	6.577	3.000	5.000	10.000
# Preclinical Projects Upon IPO	258	4.791	4.496	2.000	4.000	7.000
# Phase-1 Projects Upon IPO	258	1.287	2.951	0.000	0.000	1.000
# Phase-2 Projects Upon IPO	258	1.043	2.366	0.000	0.000	1.000
# Phase-3 Projects Upon IPO	258	0.155	0.506	0.000	0.000	0.000
% Projects Suspended before IPO	258	33.907	25.905	9.091	33.333	52.500
% Preclinical Projects Upon IPO	258	67.119	33.244	50.000	75.000	100.000
% Phase-1 Projects Upon IPO	258	13.364	20.772	0.000	0.000	23.077
% Phase-2 Projects Upon IPO	258	14.996	25.086	0.000	0.000	23.077
% Phase-3 Projects Upon IPO	258	4.521	17.134	0.000	0.000	0.000

Table 3: VC activism and board representation

This table shows the results of Equation (1) with Cortellis drug companies from 2000Q1 to 2020Q4. The unit of observation is a drug company × year-quarter combination. The dependent variable is *New board*, which is a dummy variable equal to one if the drug company has any new board members from its VC investors in a given quarter. *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI* is the investment-amount-weighted HHI index for a drug company's investing VCs; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *# Developing Drugs* denotes the number of drugs under active development from a drug company. The VC investment data to construct VC activism intensity measures and board entrance indicators is collected from Pitchbook. The IPO dates for drug companies are sourced from SDC Platinum and supplemented by Jay Ritter's IPO data. All columns include company and year-quarter fixed effects. Standard errors are double clustered at company and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	New Board			
	(1)	(2)	(3)	(4)
Ln(EW-Size)	-0.008***			
	(-2.96)			
Ln(VW-Size)		-0.007**		
		(-2.49)		
EW-HHI			0.042***	
			(3.49)	
VW-HHI				0.037***
				(3.08)
Ln(VC Amount)	0.012***	0.012***	0.011***	0.011***
	(4.81)	(4.78)	(4.53)	(4.55)
# Developing Drugs	-0.001	-0.001	-0.001	-0.001
	(-1.09)	(-1.06)	(-1.06)	(-1.07)
Company FE	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes
Founded Year FE	0.0323	0.0322	0.0325	0.0323
Adjusted R^2	19,748	19,748	19,748	19,748

Table 4: VC activism and life science startup IPO exits

This table shows the relation between investor activism and life science startup IPOs from 2000Q1 to 2020Q4. As a cross-sectional analysis, the unit of observation is a drug company. The dependent variable is *IPO*, which is a dummy variable equal to one if the drug company exits via IPOs within the sample period. For both the simple mean and weighted mean (by investment amount) of a drug company's investing VC portfolio sizes (*EW-Size* and *VW-Size*), we first take the time-series average across the sample period of a focal company. We then take the logarithm to generate *Ln(EW-Size)* and *Ln(VW-Size)*. The equal-weighted and the investment-amount-weighted HHI indexes, *EW-HHI* and *VW-HHI*, are also averaged across the sample period of a focal company. *Ln(Avg VC Amount)* is the logarithm of the average investment amount for a drug company over the sample period. The VC investment data to construct VC activism intensity measures is collected from Pitchbook. The IPO dates for drug companies are sourced from SDC Platinum and supplemented by Jay Ritter's IPO data. All columns include ICD-9, drug company founded year, and startup headquarters fixed effects. Standard errors are double clustered at ICD-9 and drug company headquarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	IPO			
	(1)	(2)	(3)	(4)
Ln(EW-Size)	0.042***			
	(3.58)			
Ln(VW-Size)		0.044***		
		(3.69)		
EW-HHI			-0.197***	
			(-3.48)	
VW-HHI				-0.212***
				(-3.60)
Ln(Avg VC Amount)	0.092***	0.091***	0.097***	0.096***
	(7.15)	(7.10)	(8.04)	(7.97)
ICD-9 FE	Yes	Yes	Yes	Yes
Startup HQ FE	Yes	Yes	Yes	Yes
Founded Year FE	Yes	Yes	Yes	Yes
Adjusted R^2	0.1819	0.1834	0.1805	0.1819
Number of observations	1,155	1,155	1,155	1,155

Table 5: VC activism and innovation progress

This table shows the results of Equation (2) using Cortellis drug development data from 2000Q1 to 2020Q4. The unit of observation is a drug-indication $\times$ year-quarter combination. The dependent variable is *Next Phase*, which is a dummy variable equal to one if the drug indication is going to progress to the next phase in the following quarter. *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI*, the investment-amount-weighted HHI index for a drug company's investing VCs; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *# Developing Drugs* denotes the number of drugs under active development from a drug company. The VC investment data to construct VC activism intensity measures is collected from Pitchbook. The IPO dates for drug companies are sourced from SDC Platinum and supplemented by Jay Ritter's IPO data. All columns include phase, drug-indication, and year-quarter fixed effects. Standard errors are double clustered at ICD-9 and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Next Phase			
	(1)	(2)	(3)	(4)
Ln(EW-Size)	0.005***			
	(3.10)			
Ln(VW-Size)		0.005***		
		(3.02)		
EW-HHI			-0.028***	
			(-3.65)	
VW-HHI				-0.026***
				(-3.32)
Ln(VC Amount)	0.002**	0.002**	0.003**	0.002**
	(2.11)	(2.03)	(2.59)	(2.49)
# Developing Drugs	-0.001	-0.001	-0.001	-0.001
	(-1.47)	(-1.45)	(-1.42)	(-1.37)
Phase FE	Yes	Yes	Yes	Yes
Drug Indication FE	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes
Adjusted R^2	0.1347	0.1347	0.1349	0.1349
Number of observations	84,123	84,123	84,123	84,123

Table 6: LP sustainability goals and VC investment strategies

This table shows the results of how VCs change investment strategies after their LPs have adopted sustainability investment goals. The unit of observation is a VC investor $\times$ year-quarter combination. We only include the sample VCs that have invested in our sample startups and have sustainability-adopting LPs and the quarterly observations in a 10-year window around the shock. In Columns (1), (3), (5) *#Com* is the logarithmic total number of companies that a VC has invested in a given industry in a given quarter; in Columns (2), (4), (6) *Amt* is the logarithmic amount of real dollar (in 2023) that a VC has invested a given industry in a given quarter. *Post* is a dummy variable equal to one after the VC's LP adopts sustainability investment goals, and zero otherwise. Columns (1) - (2), (3) - (4), and (5) - (6) report the results for VC investment in the energy, health and financial sector, respectively. The VC investment data is collected from Pitchbook. The GDP price deflator data to deflate VC investment amount over time is sourced from the U.S. Federal Reserve. All columns include investor fixed effects. Standard errors are double clustered at investor and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Energy		*Healthcare*		*Financial*	
	# Com	*Amt*	*# Com*	*Amt*	*# Com*	*Amt*
	(1)	(2)	(3)	(4)	(5)	(6)
Post	-0.021***	-0.062***	0.018	0.079	0.013*	0.042*
	(-3.33)	(-3.23)	(0.74)	(1.39)	(1.95)	(1.97)
Investor FE	Yes	Yes	Yes	Yes	Yes	Yes
Adjusted R^2	0.1770	0.1342	0.5323	0.5068	0.1994	0.1688
Number of observations	4,309	4,309	4,309	4,309	4,309	4,309

Table 7: Instrumented VC activism and innovation progress

This table shows the 2SLS results of Equation (2) using an instrument based on LPs' ESG investment preference. The unit of observation is a drug-indication×year-quarter combination. *Weighted Exposure* is the share of holding VCs exposed to the sustainability shock of a focal startup. Columns (1) - (4) report the first-stage regression results for the VC activism intensity measures in Table 5: *Ln(EW-Size)*, *Ln(VW-Size)*, *EW-HHI* and *VW-HHI*. Columns (5) - (8) report the second-stage regression results using four instrumented VC activism intensity measures. The dependent variable is *Next Phase*, which is a dummy variable equal to one if the drug indication is going to progress to the next phase in the following quarter. *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years. *# Developing Drugs* denotes the number of drugs under active development from a drug company. The VC investment data to construct VC activism intensity measures is collected from Pitchbook. The IPO dates for drug companies are sourced from SDC Platinum and supplemented by Jay Ritter's IPO data. All columns include phase, drug-indication, and year-quarter fixed effects. Standard errors are double clustered at ICD-9 and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Ln(EW-Size)	*Ln(VW-Size)*	*EW-HHI*	*VW-HHI*	*Next Phase*			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Weighted Exposure	-0.729***	-0.703***	0.058***	0.052***				
	(-6.67)	(-6.77)	(3.57)	(3.40)				
$\widehat{\textit{Ln(EW-Size)}}$					0.035***			
					(2.67)			
$\widehat{\textit{Ln(VW-Size)}}$						0.036**		
						(2.60)		
$\widehat{\textit{EW-HHI}}$							-0.441**	
							(-2.17)	
$\widehat{\textit{VW-HHI}}$								-0.494**
								(-2.13)
Ln(VC Amount)	0.053***	0.070***	0.011***	0.007**	0.000	-0.000	0.007***	0.006***
	(3.44)	(4.15)	(4.00)	(2.45)	(0.24)	(-0.17)	(2.97)	(2.68)
# Developing Drugs	-0.017***	-0.019***	0.004***	0.005***	-0.000	-0.000	0.001	0.002
	(-3.42)	(-3.72)	(3.58)	(4.36)	(-0.16)	(-0.02)	(1.04)	(1.32)
Drug Indication FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Phase FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Kleibergen-Paap F-test	44.47	45.77	12.71	11.53	-	-	-	-
Adjusted R^2	0.012	0.017	0.008	0.007	–	–	–	–
Observations	84,123	84,123	84,123	84,123	84,123	84,123	84,123	84,123

Table 8: VC activism and project discontinuation due to pipeline priority

This table shows the results of Equation (3) with a sub-sample of discontinued projects from 2000Q1 to 2020Q4. The unit of observation is the drug indication. The dependent variable is *Pipeline Priority*, which is a dummy variable equal to one if the drug indication is discontinued due to pipeline priority. *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI* is the investment-amount-weighted HHI index for a drug company's investing VCs; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *Ln(# Indications)* is the logarithmic one plus the number of indications under active development from a focal drug. The VC investment data to construct VC activism intensity measures is collected from Pitchbook. The IPO dates for drug companies are sourced from SDC Platinum and supplemented by Jay Ritter's IPO data. All columns include ICD-9, startup-founded year, and headquarters fixed effects. Standard errors are double clustered at ICD-9 and drug company headquarters level; t statistics are in parentheses; $^{*}p < 0.05$,** $p < 0.01$,*** $p < 0.001$.

	Pipeline Priority			
	(1)	(2)	(3)	(4)
Ln(EW-Size)	-0.107**			
	(-2.47)			
Ln(VW-Size)		-0.107**		
		(-2.56)		
EW-HHI			0.902*	
			(1.97)	
VW-HHI				0.913*
				(1.93)
Ln(VC Amount)	0.019	0.019	-0.008	-0.003
	(0.51)	(0.48)	(-0.22)	(-0.08)
# Indications	-0.277***	-0.278***	-0.276**	-0.280**
	(-2.74)	(-2.76)	(-2.59)	(-2.60)
ICD-9 FE	Yes	Yes	Yes	Yes
Found Yr FE	Yes	Yes	Yes	Yes
Startup HQ FE	Yes	Yes	Yes	Yes
Adjusted R^2	0.5228	0.5240	0.5337	0.5332
Number of observations	194	194	194	194

Table 9: VC activism and innovation progress: heterogeneity due to R&D stages

This table shows the results of Equation (2) in subsamples split by R&D stages. The unit of observation is a drug-indication×year-quarter combination. Columns (1)-(4) report the results with pre-clinical phase and Phase 1 records and column (5)-(8) report the results with Phase 2 and Phase 3 records. The dependent variable is *Next Phase*, which is a dummy variable equal to one if the drug indication is going to progress to the next phase in the following quarter. *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI* is the investment-amount-weighted HHI index for a drug company's investing VCs; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *# Developing Drugs* denotes the number of drugs under active development from a drug company. The VC investment data to construct VC activism intensity measures is collected from Pitchbook. The IPO dates for drug companies are sourced from SDC Platinum and supplemented by Jay Ritter's IPO data. All columns include phase, drug-indication, and year-quarter fixed effects. Standard errors are double clustered at ICD-9 and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Next Phase							
	Preclinical Phase & Phase 1				*Phase 2 & Phase 3*			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Ln(EW-Size)	0.003**				0.003			
	(2.28)				(1.13)			
Ln(VW-Size)		0.003**				0.003		
		(2.18)				(0.99)		
EW-HHI			-0.017***				-0.010	
			(-3.16)				(-1.06)	
VW-HHI				-0.017***				-0.008
				(-2.84)				(-0.83)
Ln(VC Amount)	0.002*	0.001	0.002**	0.002*	0.004	0.004	0.004	0.004
	(1.68)	(1.62)	(2.01)	(1.92)	(1.39)	(1.40)	(1.42)	(1.41)
# Developing Drugs	-0.000	-0.000	-0.000	-0.000	-0.003***	-0.002***	-0.002***	-0.002***
	(-0.65)	(-0.65)	(-0.64)	(-0.62)	(-3.15)	(-3.12)	(-3.04)	(-3.02)
Phase FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Drug Indication FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Adjusted R^2	0.1380	0.1380	0.1381	0.1381	0.1053	0.1052	0.1052	0.1052
Number of observations	72,031	72,031	72,031	72,031	11,963	11,963	11,963	11,963

Table 10: VC activism and innovation progress: heterogeneity due to regulatory designations

This table shows the results of Equation (2) in subsamples split by orphan drug designations. The unit of observation is a drug-indication×year-quarter combination. Columns (1) - (4) report the results with drug indications that ever have obtained orphan drug designations; columns (5) - (8) report the results with drug indications that never have obtained orphan drug designations. The dependent variable is *Next Phase*, which is a dummy variable equal to one if the drug indication is going to progress to the next phase in the following quarter. *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI* is the investment-amount-weighted HHI index for a drug company's investing VCs; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *# Developing Drugs* denotes the number of drugs under active development from a drug company. The VC investment data to construct VC activism intensity measures is collected from Pitchbook. The IPO dates for drug companies are sourced from SDC Platinum and supplemented by Jay Ritter's IPO data. All columns include phase, drug-indication, and year-quarter fixed effects. Standard errors are double clustered at ICD-9 and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Next Phase							
	Focal-orphan Drug Indications				*Non-orphan Drug Indications*			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
EW-Ln(# Startups)	-0.007				0.005**			
	(-0.57)				(2.37)			
VW-Ln(# Startups)		-0.008				0.004**		
		(-0.66)				(2.28)		
EW-HHI(Startups)			0.006				-0.033***	
			(0.09)				(-3.21)	
VW-HHI(Startups)				0.018				-0.031***
				(0.26)				(-2.90)
Ln(VC Amount)	0.001	0.001	0.001	0.001	0.002**	0.002**	0.003***	0.003***
	(0.20)	(0.19)	(0.23)	(0.20)	(2.42)	(2.35)	(2.94)	(2.84)
# Developing Drugs	-0.002	-0.002	-0.002	-0.002	-0.001	-0.001	-0.001	-0.001
	(-0.39)	(-0.39)	(-0.37)	(-0.37)	(-1.57)	(-1.54)	(-1.50)	(-1.42)
Phase FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Drug Indication FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Adjusted R^2	0.1085	0.1086	0.1084	0.1084	0.1097	0.1097	0.1101	0.1101
Number of observations	2,750	2,750	2,750	2,750	62,833	62,833	62,833	62,833

Table 11: VC activism and innovation progress: heterogeneity due to experimentation length

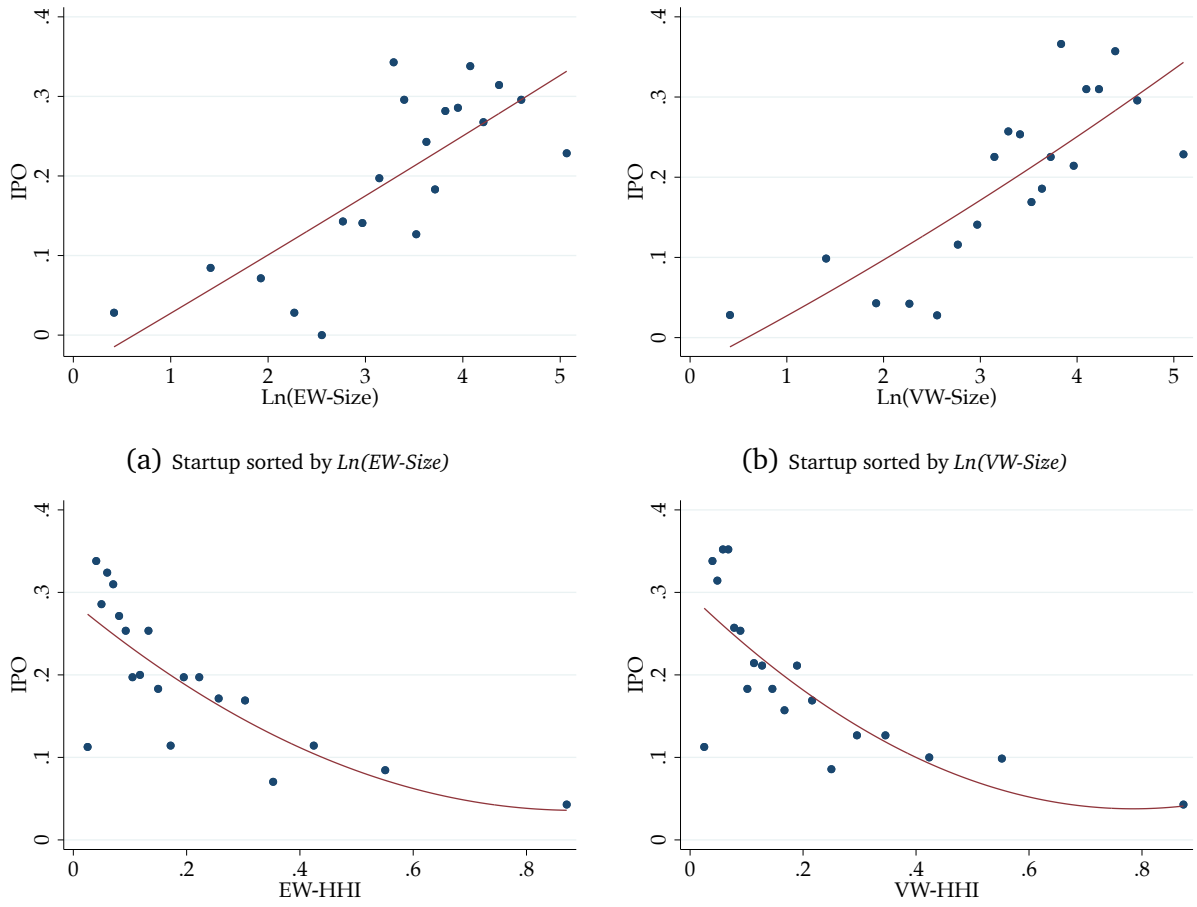
This table shows the results of Equation (2) in subsamples split by experimentation length. The unit of observation is a drug-indication×year-quarter combination. Columns (1) - (4) report the results with drug indications from ICD-9 classifications that have below-median developing lengths; columns (5) - (8) report the results with drug indications from ICD-9 classifications that have above-median developing lengths. The dependent variable is *Next Phase*, which is a dummy variable equal to one if the drug indication is going to progress to the next phase in the following quarter. *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI* is the investment-amount-weighted HHI index for a drug company's investing VCs; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *# Developing Drugs* denotes the number of drugs under active development from a drug company. The VC investment data to construct VC activism intensity measures is collected from Pitchbook. The IPO dates for drug companies are sourced from SDC Platinum and supplemented by Jay Ritter's IPO data. All columns include phase, drug-indication, and year-quarter fixed effects. Standard errors are double clustered at ICD-9 and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Next Phase							
	Fast ICD-9 Drug Indications				*Slow ICD-9 Drug Indications*			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
EW-Size	0.002				0.006***			
	(0.74)				(3.80)			
VW-Size		0.002				0.006***		
		(0.82)				(3.69)		
EW-HHI			-0.022*				-0.030***	
			(-1.97)				(-4.28)	
VW-HHI				-0.024*				-0.027***
				(-1.85)				(-3.99)
Ln(VC Amount)	0.001	0.001	0.001	0.001	0.003**	0.003**	0.003***	0.003***
	(0.69)	(0.66)	(0.84)	(0.82)	(2.47)	(2.40)	(3.11)	(2.93)
# Developing Drugs	0.000	0.000	0.000	0.000	-0.001**	-0.001**	-0.001**	-0.001**
	(0.41)	(0.41)	(0.42)	(0.44)	(-2.39)	(-2.37)	(-2.32)	(-2.26)
Phase FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Drug Indication FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Adjusted R^2	0.1370	0.1370	0.1371	0.1372	0.1332	0.1332	0.1333	0.1332
Number of observations	32,595	32,595	32,595	32,595	51,528	51,528	51,528	51,528

Table 12: VC activism and therapeutic area concentration

This table shows the relation between VC activism and startup therapeutic area concentration. The unit of observation is a drug-indication $\times$ year-quarter combination. For each focal project, *Own Share* is the fraction of other projects developed by its firm in the same ICD area over all the projects held by its VC investors. *Competitor Share* is the fraction of other projects developed by other commonly-owned startups in the same ICD area over all the projects held by its VC investors. A commonly-owned startup is another startup invested by a focal startup's VC investors. *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI*, the investment-amount-weighted HHI index for a drug company's investing VCs; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *# Developing Drugs* denotes the number of drugs under active development from a drug company. The VC investment data to construct VC activism intensity measures is collected from Pitchbook. The IPO dates for drug companies are sourced from SDC Platinum and supplemented by Jay Ritter's IPO data. All columns include phase, drug-indication, and year-quarter fixed effects. Standard errors are double clustered at ICD-9 and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Own Share				*Competitor Share*			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Ln(EW-Size)	-0.011***				0.004**			
	(-2.86)				(2.26)			
Ln(VW-Size)		-0.010***				0.004**		
		(-2.84)				(2.13)		
EW-HHI			0.046***				-0.020**	
			(4.13)				(-2.15)	
VW-HHI				0.044***				-0.018**
				(4.45)				(-2.08)
Ln(VC Amount)	-0.001	-0.000	-0.002	-0.001	0.000	0.000	0.001*	0.001
	(-0.26)	(-0.22)	(-0.78)	(-0.71)	(1.00)	(0.95)	(1.67)	(1.61)
# Developing Drugs	0.003***	0.003***	0.003***	0.003***	-0.000	-0.000	-0.000	-0.000
	(3.90)	(3.90)	(3.86)	(3.80)	(-1.33)	(-1.36)	(-1.36)	(-1.37)
Phase FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Drug Indication FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Number of obs.	84,123	84,123	84,123	84,123	84,123	84,123	84,123	84,123
Adjusted R^2	0.8547	0.8545	0.8547	0.8546	0.8182	0.8180	0.8183	0.8181



(a) Startup sorted by *Ln(EW-Size)*

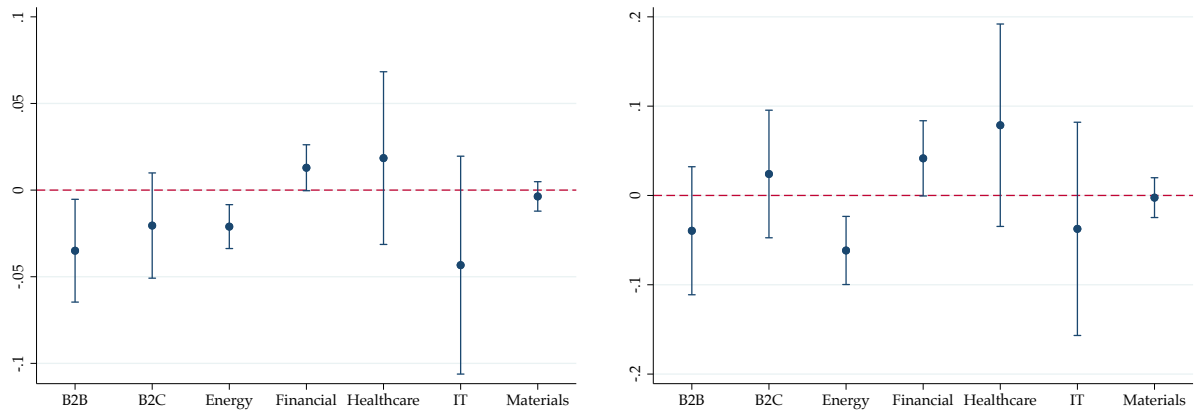
(b) Startup sorted by *Ln(VW-Size)*

(c) Startup sorted by *EW-HHI*

(d) Startup sorted by *VW-HHI*

Figure 1: **VC activism and life science startup IPO outcomes**

Figure 1 shows the relation between VC activism and life-science startup IPO probability from 2000Q1 to 2020Q4. In each figure, all startups are sorted into 20 equal-size bins with similar levels of VC activism intensity over the sample period. Figures 1a to 1d measure VC activism intensity with *Ln(EW-Size)*, *Ln(VW-Size)*, *EW-HHI*, and *VW-HHI*, respectively. The y-axis indicates the fraction of IPO startups within each bin. Each red curve plots the fitted quadratic regression for VC activism and IPOs. The project development status data is sourced from Cortellis. The VC investment data to construct VC activism intensity measures is collected from Pitchbook. The IPO dates for drug companies are sourced from SDC Platinum and supplemented by Jay Ritter's IPO data.



(a) Total number of companies within an industry

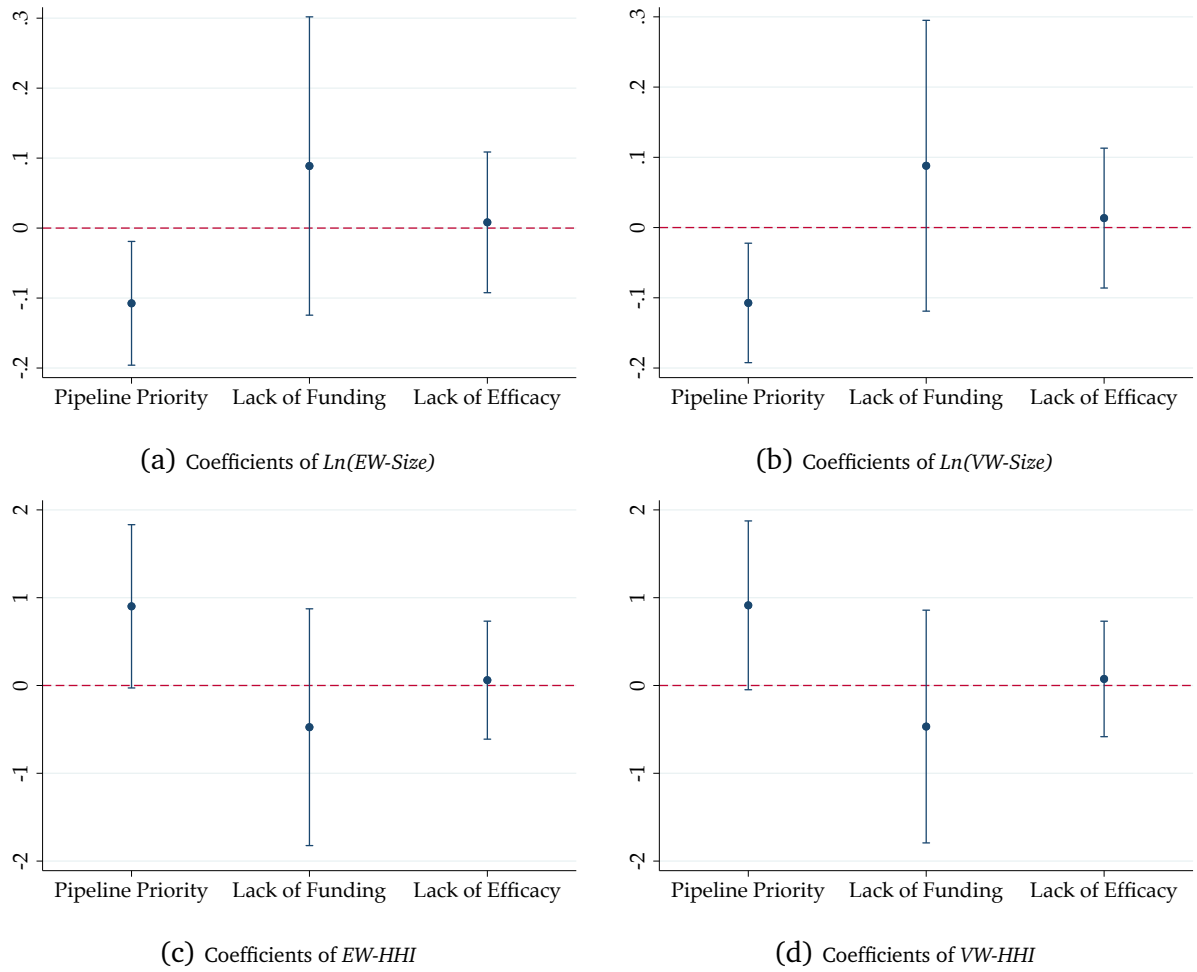
(b) Total amount of real dollar within an industry

Figure 2: **LP sustainability goals and VC investment strategies**

Figure 3 shows the change in industry-level investment strategies for VCs with LPs adopting sustainability investment goals in a 10-year window around the shock. Each figure plots the coefficients of *Post* (i.e., β) by estimating the following regression for VC investment in industries of *Business Products and Services (B2B)*, *Consumer Products and Services (B2C)*, *Energy*, *Financial Services (Financial)*, *Healthcare*, *Information Technology (IT)* and *Materials and Resources (Materials)*:

$$VC\,Investment_{j,t} = \alpha + \beta Post_{j,t} + FE + \epsilon_{j,t}.$$

Figures 2a and 2b measure VC investment with *Ln(number of companies)*, and *Ln(amount of real dollar)*, respectively. The error bars denote 95% confidence intervals. The VC investment data is collected from Pitchbook. The GDP price deflator data to deflate VC investment amount over time is sourced from the U.S. Federal Reserve.



(a) Coefficients of *Ln(EW-Size)*

(b) Coefficients of *Ln(VW-Size)*

(c) Coefficients of *EW-HHI*

(d) Coefficients of *VW-HHI*

Figure 3: **VC activism and drug project discontinuation**

Figure 3 shows the relation between VC activism intensity and drug project discontinuation from 2000Q1 to 2020Q4. Each figure plots the coefficients of *VC Activism* (i.e., β) by estimating the following regression for discontinuation reasons of *pipeline priority* , *lack of funding* and *lack of efficacy*:

$$Reason_{i,j,k,t} = \alpha + \beta VC\ Activism_{k,t} + \Phi X_{k,t} + FEs + \epsilon_{i,j,k,l}.$$

Figures 3a to 3d measure VC activism intensity with *Ln(EW-Size)*, *Ln(VW-Size)*, *EW-HHI*, and *VW-HHI*, respectively. The error bars denote 95% confidence intervals. The project development status and discontinuation data are sourced from Cortellis. The VC investment data to construct VC activism intensity measures is collected from Pitchbook.

Internet Appendix to "How Does VC Activism Backfire in Startup Experimentation?"

Table IA.1: Summary statistics by R&D stages

This table replicates the summary statistics of Table 1 by splitting the sample into early and late stages. Panel A reports the statistics for projects in the pre-clinical phase or Phase 1, and Panel B reports the statistics for projects in Phase 2 or Phase 3. The other details are the same as Table 1.

	Obs.	Mean	STD	p25	Median	p75
Panel A: Pre-clinical Phase & Phase 1						
Next Phase	72,756	0.014	0.117	0.000	0.000	0.000
EW-Size	72,756	39.533	40.896	13.000	29.167	51.200
Ln(EW-Size)	72,756	3.173	1.135	2.565	3.373	3.936
VW-Size	72,756	40.664	42.974	13.000	30.000	52.847
Ln(VW-Size)	72,756	3.188	1.148	2.565	3.401	3.967
EW-HHI	72,756	0.220	0.218	0.068	0.141	0.290
VW-HHI	72,756	0.216	0.219	0.067	0.135	0.286
VC Amount (in millions)	72,756	28.792	41.035	5.640	15.989	37.500
Ln(VC Amount)	72,756	16.355	1.526	15.545	16.587	17.440
# Developing Drugs	72,756	7.026	6.073	3.000	5.000	9.000
Panel B: Phase 2 & Phase 3						
Next Phase	12,090	0.008	0.088	0.000	0.000	0.000
EW-Size	12,090	36.638	44.684	9.286	26.250	46.250
Ln(EW-Size)	12,090	2.996	1.233	2.228	3.268	3.834
VW-Size	12,090	37.624	47.534	9.000	26.200	47.000
Ln(VW-Size)	12,090	2.999	1.249	2.197	3.266	3.850
EW-HHI	12,090	0.249	0.244	0.074	0.155	0.340
VW-HHI	12,090	0.248	0.247	0.072	0.148	0.334
VC Amount (in millions)	12,090	31.233	43.005	7.776	20.289	38.236
Ln(VC Amount)	12,090	16.615	1.286	15.867	16.826	17.459
# Developing Drugs	12,090	6.809	6.036	3.000	5.000	9.000

Table IA.2: Robustness of standard errors clustered at company and year-quarter level

This table shows the results of Equation (2) using Cortellis drug development data from 2000Q1 to 2020Q4. The details are the same as Table 5, except that standard errors are double clustered at company and year-quarter levels. All columns include phase, drug-indication, and year-quarter fixed effects. t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Next Phase			
	(1)	(2)	(3)	(4)
Ln(EW-Size)	0.005***			
	(2.71)			
Ln(VW-Size)		0.005**		
		(2.63)		
EW-HHI			-0.028***	
			(-3.13)	
VW-HHI				-0.026***
				(-2.88)
Ln(VC Amount)	0.002**	0.002**	0.003***	0.002**
	(2.09)	(2.01)	(2.67)	(2.55)
# Developing Drugs	-0.001	-0.001	-0.001	-0.001
	(-1.21)	(-1.20)	(-1.19)	(-1.15)
Phase FE	Yes	Yes	Yes	Yes
Drug Indication FE	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes
Adjusted R^2	0.1347	0.1347	0.1349	0.1349
Number of observations	84,123	84,123	84,123	84,123

Table IA.3: Robustness of standard errors clustered at ICD-chapter and year-quarter level

This table shows the results of Equation (2) using Cortellis drug development data from 2000Q1 to 2020Q4. The details are the same as Table 5, except that standard errors are double clustered at ICD-chapter and year-quarter levels. All columns include phase, drug-indication, and year-quarter fixed effects. t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Next Phase			
	(1)	(2)	(3)	(4)
Ln(EW-Size)	0.005***			
	(3.10)			
Ln(VW-Size)		0.005***		
		(3.04)		
EW-HHI			-0.028***	
			(-3.59)	
VW-HHI				-0.026***
				(-3.30)
Ln(VC Amount)	0.002**	0.002**	0.003***	0.002***
	(2.38)	(2.28)	(2.94)	(2.81)
# Developing Drugs	-0.001	-0.001	-0.001	-0.001
	(-1.39)	(-1.38)	(-1.35)	(-1.30)
Phase FE	Yes	Yes	Yes	Yes
Drug Indication FE	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes
Adjusted R^2	0.1347	0.1347	0.1349	0.1349
Number of observations	84,123	84,123	84,123	84,123

Table IA.4: VC activism and project discontinuation due to other reasons

This table shows the results of Equation (3) for other discontinuation reasons. The unit of observation is the drug indication. The dependent variable in columns (1) - (4) is *Lack of Funding*, which is a dummy variable equal to one if the drug indication is discontinued due to lack of funding; the dependent variable in columns (5) - (8) is *Lack of Efficacy*, which is a dummy variable equal to one if the drug indication is discontinued due to lack of efficacy. *Ln(EW-Size)* is the logarithmic number of the simple mean of a drug company's investing VC portfolio sizes; *Ln(VW-Size)* is the logarithmic number of the weighted mean (by investment amount) of a drug company's investing VC portfolio sizes; *EW-HHI* is the simple average of the HHI index for a drug company's investing VCs; *VW-HHI* is the investment-amount-weighted HHI index for a drug company's investing VCs; *Ln(VCAmount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *Ln(# Indications)* is the logarithmic one plus the number of indications under active development from a drug. The VC investment data to construct VC activism intensity measures is collected from Pitchbook. The IPO dates for drug companies are sourced from SDC Platinum and supplemented by Jay Ritter's IPO data. All columns include the 9th International Classification of Diseases (ICD-9), startup-founded year, and headquarters fixed effects. Standard errors are double clustered at ICD-9 level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Discontinuation Reason							
	Lack of Funding				*Lack of Efficacy*			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Ln(EW-Size)	0.089				0.008			
	(0.84)				(0.17)			
Ln(VW-Size)		0.088				0.013		
		(0.86)				(0.27)		
EW-HHI			-0.475				0.061	
			(-0.71)				(0.18)	
VW-HHI				-0.468				0.074
				(-0.72)				(0.23)
Ln(VC Amount)	-0.047	-0.046	-0.021	-0.024	0.093***	0.091***	0.096***	0.097***
	(-0.85)	(-0.84)	(-0.48)	(-0.53)	(3.64)	(3.56)	(3.67)	(3.74)
# Indications	0.212*	0.213*	0.203*	0.204*	0.205*	0.206*	0.201	0.200
	(1.93)	(1.93)	(1.79)	(1.82)	(1.71)	(1.73)	(1.63)	(1.64)
ICD-9 FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Found Year FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Startup HQ FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Adjusted R^2	0.4377	0.4380	0.4298	0.4292	0.4694	0.4697	0.4694	0.4694
Number of observations	194	194	194	194	194	194	194	194

Table IA.5: The relationship between lead VC activism and drug development status

This table shows the results of Equation (2) with lead VC activism. The unit of observation is a drug-indication×year-quarter combination. The dependent variable is *Next Phase*, which is a dummy variable equal to one if the drug indication is going to progress to the next phase in the following quarter. *Ln(Lead VC Size)* is the logarithmic number of a drug company's lead VC's portfolio sizes; *Lead VC HHI* is the the HHI index for a drug company's lead VC's portfolio; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *# Developing Drugs* denotes the number of drugs under active development from a drug company. A drug company's lead VC in a given quarter is defined as the VC investor who has made the most investment in the company over the past five years. The VC investment data to construct VC activism intensity measures is collected from Pitchbook. The IPO dates for drug companies are sourced from SDC Platinum and supplemented by Jay Ritter's IPO data. All columns include phase, drug-indication, and year-quarter fixed effects. Standard errors are clustered at ICD-9 and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05$,** $p < 0.01$,*** $p < 0.001$.

	Next Phase	
	(1)	(2)
Ln(Lead VC Size)	0.005***	
	(2.73)	
Lead VC HHI		-0.021**
		(-2.51)
Ln(VC Amount)	0.002**	0.002**
	(2.18)	(2.23)
# Developing Drugs	-0.001	-0.001
	(-1.49)	(-1.47)
Phase FE	Yes	Yes
Drug Indication FE	Yes	Yes
Year-Quarter FE	Yes	Yes
Adjusted R^2	0.1348	0.1348
Number of observations	84,123	84,123

Table IA.6: VC activism and innovation progress (industry concentration)

This table shows the results of Equation (2) using Cortellis drug development data from 2000Q1 to 2020Q4. The details are the same as Table 5, except that VC activism intensity measures are constructed at the portfolio company industry level. All columns include phase, drug-indication and year-quarter fixed effects. Standard errors are clustered at ICD-9 and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05$,** $p < 0.01$,*** $p < 0.001$.

	Next Phase			
	(1)	(2)	(3)	(4)
Ln(EW-Size)	0.007***			
	(2.81)			
Ln(VW-Size)		0.007***		
		(2.79)		
EW-HHI			-0.022***	
			(-2.95)	
VW-HHI				-0.020***
				(-2.70)
Ln(VC Amount)	0.002**	0.002**	0.003***	0.003**
	(2.38)	(2.31)	(2.72)	(2.63)
# Developing Drugs	-0.001	-0.001	-0.001	-0.001
	(-1.39)	(-1.38)	(-1.37)	(-1.37)
Phase FE	Yes	Yes	Yes	Yes
Drug Indication FE	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes
Adjusted R^2	0.1347	0.1347	0.1347	0.1347
Number of observations	84,123	84,123	84,123	84,123

Table IA.7: VC activism and innovation progress (geographic concentration)

This table shows the results of Equation (2) using Cortellis drug development data from 2000Q1 to 2020Q4. The details are the same as Table 5, except that VC activism intensity measures are constructed at the portfolio company headquarter state level. All columns include phase, drug-indication and year-quarter fixed effects. Standard errors are clustered at ICD-9 and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05$,** $p < 0.01$,*** $p < 0.001$.

	Next Phase			
	(1)	(2)	(3)	(4)
Ln(EW-Size)	0.007***			
	(3.10)			
Ln(VW-Size)		0.008***		
		(3.13)		
EW-HHI			-0.023***	
			(-2.65)	
VW-HHI				-0.023**
				(-2.59)
Ln(VC Amount)	0.002**	0.002*	0.002**	0.002*
	(2.02)	(1.91)	(2.01)	(1.94)
# Developing Drugs	-0.001	-0.001	-0.001*	-0.001*
	(-1.47)	(-1.42)	(-1.72)	(-1.66)
Phase FE	Yes	Yes	Yes	Yes
Drug Indication FE	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes
Adjusted R^2	0.1347	0.1348	0.1348	0.1348
Number of observations	84,123	84,123	84,123	84,123

Table IA.8: VC activism and innovation progress using VentureXpert data

This table shows the results of Equation (2) using the VentureXpert data. The details are the same as Table 5, except that the VC investment data to construct VC activism intensity measures is collected from VentureXpert. All columns include phase, drug-indication, and year-quarter fixed effects. Standard errors are double clustered at ICD-9 and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Next Phase			
	(1)	(2)	(3)	(4)
Ln(EW-Size)	0.003**			
	(2.37)			
Ln(VW-Size)		0.004***		
		(3.04)		
EW-HHI			-0.015**	
			(-2.13)	
VW-HHI				-0.016**
				(-2.23)
Ln(VC Amount)	0.002***	0.002***	0.002***	0.002***
	(2.84)	(2.76)	(3.12)	(3.08)
# Developing Drugs	-0.001**	-0.001**	-0.001**	-0.001**
	(-2.17)	(-2.19)	(-2.18)	(-2.18)
Phase FE	Yes	Yes	Yes	Yes
Drug Indication FE	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes
Adjusted R^2	0.1184	0.1185	0.1184	0.1184
Number of observations	97,226	97,226	97,226	97,226

Table IA.9: Flight-induced VC engagement and innovation progress

This table shows the results of Equation (4) using Cortellis drug development data from 2000Q1 to 2020Q4. The unit of observation is a drug-indication×year-quarter combination. Columns (1)-(2) report the full sample results; columns (3)-(4) report the results with pre-clinical and Phase 1 projects; columns (5)-(6) report the results with Phase 2 and Phase 3 projects. Columns (1), (3), (5) use the OLS estimator; Columns (2), (4), (6) report the post-treatment average IW estimators proposed by Sun and Abraham (2021). The dependent variable is *Next Phase*, which is a dummy variable equal to one if the drug indication is going to progress to the next phase in the following quarter. *Lead VC-treated* is a dummy variable equal to one if direct flights between a drug company's headquarters and its lead VC's headquarters have become available by quarter t; *Ln(VC Amount)* is the logarithmic aggregated investment amount made by all VC investors to the drug company in the past three years; *# Developing Drugs* is the number of drugs under active development from the drug company in a given quarter; *# Quarters since first inv* is the number of quarters since first investment from a drug startup's lead investor. The US airline route data to construct *Lead VC-treated* is collected from T-100 Domestic Segments data maintained by the Bureau of Transportation Statistics. All columns include phase, drug-indication, and year-quarter fixed effects. Standard errors are clustered at ICD-9 and year-quarter level; t statistics are in parentheses; $^{*}p < 0.05, ^{**}p < 0.01, ^{***}p < 0.001$.

	Next Phase					
	All Phases		*Preclinical & Phase 1*		*Phase 2 & Phase 3*	
	(1)	(2)	(3)	(4)	(5)	(6)
Lead VC-treated	-0.006	-0.008**	-0.009**	-0.013***	0.000	0.006
	(-1.32)	(-2.25)	(-1.99)	(-6.11)	(0.03)	(0.89)
Ln(VC Amount)	0.003**		0.002*		0.006*	
	(2.57)		(1.91)		(1.93)	
# Developing drugs	-0.001		-0.000		-0.003***	
	(-1.57)		(-0.74)		(-3.40)	
# Quarters since first inv	0.000		0.000		0.001***	
	(1.42)		(0.48)		(2.66)	
Drug Indication FE	Yes	Yes	Yes	Yes	Yes	Yes
Phase FE	Yes	Yes	Yes	Yes	Yes	Yes
Year-Quarter FE	Yes	Yes	Yes	Yes	Yes	Yes
Adjusted R^2	0.1346	0.1233	0.1380	0.1260	0.1061	0.0614
Number of observations	84,123	84,123	72,031	72,031	11,963	11,963

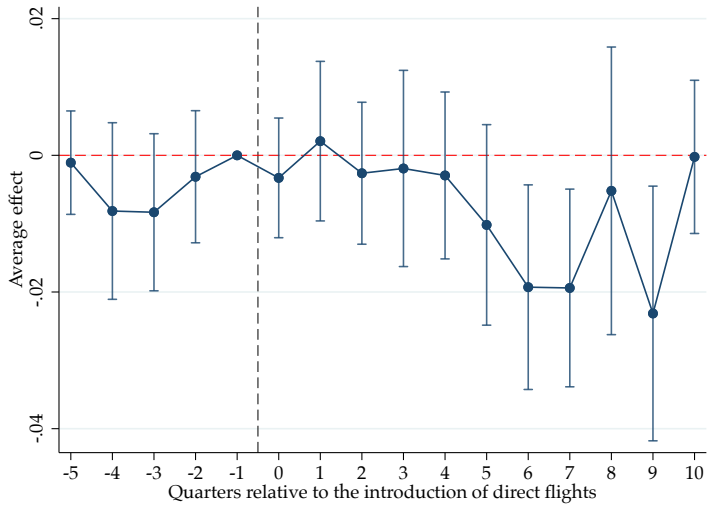


Figure IA.1: **Impacts of direct flights on drug development progress**

Figure IA.1 shows the event-study plots of the following equation using IW estimators proposed by Sun and Abraham (2021):

$$Next\,Phase_{i,j,k,p,t} = \alpha + \sum_{s=-5}^{10} \beta_s D_{s(k,t)} + \Phi X_{k,t} + \gamma_{i,j} + \delta_p + \zeta_t + \epsilon_{i,j,k,p,t}$$

The dependent variable is $Next\,Phase_{i,j,k,p,t}$, which is a dummy variable equal to one if indication i of drug j at phase p from company k enters next phase at time $t+1$. The key independent variable $D_{s(kt)}$ is a collection of indicator variables equal to one if for drug company k at time t, the introduction of a direct flight between k and its lead investor is s quarters away. The drug development progress data is collected from Cortellis. The US domestic direct flight data to construct treatment dummies is collected from T-100. Both figures include phase, drug-indication, and year-quarter fixed effects. The bars represent 95 percent confidence intervals. Standard errors are double clustered at drug company and year-quarter level.